

Journal of IiMER

I N V E S T i n M E
R E S E A R C H

Journal Of IiMER



MAY 2017 VOLUME 11 ISSUE 1

**UK Charity Invest in ME Research
(Charity Nr. 1153730)**

RESEARCH into ME?

WE NEEDED A RETHINK



www.investinme.org

Small charity BIG Cause

With no major investment into correct research into myalgic encephalomyelitis during the last decades Invest in ME Research has, with a determined band of supporters, taken action for change in the absence of any coherent or scientific establishment policies.

Funding has to be given to biomedical research and new knowledge from other disciplines such as virology, immunology, endocrinology etc. has to be brought in to help research into ME.

Invest in ME Research has initiated and funded high-quality biomedical research at UCL and UEA and Quadram Institute Biosciences - and brought in collaborations with other researchers in Bergen, Uppsala, Berlin and within the UK in Oxford.

Vision with action can change the world

Journal of liMER

MAY 2017



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IIMEC12: Marking TWELVE Years in Creating a Vision of Excellence for Research into ME

Conference welcome from Chairman

Kathleen McCall

Another year
and a new conference.



Invest in ME Research is an independent UK charity whose objectives are to initiate, maintain and augment a strategy of high-quality biomedical research into Myalgic Encephalomyelitis (ME), to provide and promote better education about ME, and to raise awareness of the effects of the disease on patients and families.

Finding, facilitating and funding a strategy of biomedical research into ME is, we believe, the only way to make any real and lasting impact on the lives of those affected by this disease.

We are a small charity but with a growing number of supporters who have big hearts - and a determination to get the best possible research to be carried out to find the cause of myalgic encephalomyelitis and develop treatments.

The charity is run by volunteers - patients or parents of children with ME and supported by patients, family, friends, and others who are determined to change the prospects for people with this disease.

We do not receive and have never received funding from government or government organisations and our research Colloquiums and public Conferences are funded by the charity itself.

The charity decided early on that biomedical research into ME was crucial in order to make progress in treating this disease. We also decided that education of healthcare staff, the media,



government departments, patient groups and patients was to be a priority.

The charity commits itself to a strong stance against deceptive practices, corrupt or flawed policies toward ME and to disingenuous posturing from those seeking to influence governments, the media or even patients.

The charity has always spoken out strongly against the flawed and null PACE Trial. However, we have also engaged with the government, Department of Health, Medical Research Council, Chief Medical Officers and, as part of the European ME Alliance (EMEA) have been working closely with European colleagues to make progress in Europe. We have also participated in recent NINDS discussions organised by the NIH.

Almost twelve years on from when Kathleen McCall formed the organisation that became Invest in ME Research the charity has an optimism about the future and a continuing determination to force change and create a foundation of biomedical research in Europe that will finally

provide answers and treatments for this disease.

Our efforts are focused on setting up a UK [Centre of Excellence for ME](#) that will provide proper examinations and diagnosis for ME patients and a coordinated strategy of translational biomedical

research into this disease.

Now our twelfth conference is taking place in 2017, as always in Westminster, London, and as the charity has embarked on a new decade of finding, funding and facilitating biomedical research into ME, and



research into ME in order to find treatment(s) and cure(s).

Our supporters have achieved an incredible feat in making something out of nothing and creating an opportunity for real progress to be attained for ME research.

Now, with solid progress made in establishing the UK Centre we can look for more rapid progress in the coming years as CDC and NIH demonstrate more acceptance of this disease and new initiatives continue to realise the charity's goal of international collaboration in research into ME. These initiatives will eventually drag and force complacent and ineffectual organisations into taking action rather than false posturing. Good collaborations have been built between UK, European, and US organisations that can only strengthen the level and quality of biomedical

increasing knowledge and awareness of the disease.

Our conferences and, later, our closed research colloquiums were organised from the beginning in order to provide a platform for research and a means of facilitating education about ME.

For Invest in ME Research, education and research are the key to progress, and hence change. The IIMER conferences have formed a crucial part of this education and our research colloquia form a crucial and productive part of the research.

The conferences now regularly attract delegates (researchers, clinicians, nurses, patient groups and patients, advocates and, we always hope, a sprinkling of as many politicians, journalists and others whom Invest in ME self-fund to allow people to be exposed to real science) from twenty countries in a unique international event that is friendly and conducive for learning and

networking.

Our choice of venue reflects our commitment to patients, families, carers, researchers and healthcare staff in providing the best venue for conducting this annual event - now [#IIMEC12](#).



For 2017, IIMEC12 brings the best from the world's Centres of Excellence for ME – now up and running as in the UK at Norwich Research Park or Australia, where the NCNED has been operating for some years, and in Norway and those being developed such as in USA.

The charity's commitment over 12 years to bringing the best research to the public and professionals has given biomedical research into ME a platform that allows researchers to overcome the bias and prejudice built up over the years by false views held by governments, research councils and establishment collaboratives that are more self-serving rather than interested in making progress.

The Invest in ME Research conferences bring together this optimism and determination in a happy mixture of wanting, needing to learn, optimism and hope that things will improve.

In June 2016, Invest in ME Research held its sixth Biomedical Research into ME Colloquium in London - BRMEC6.

The Colloquium had as its theme international collaboration.

Our Colloquium banner used the quote attributed to Henry Ford to describe the progress made –

***"Coming together is a beginning;
keeping together is progress;
working together is success"***

Our invited delegates (researchers from 14 countries around the world) embraced this theme.

The BRMEC6 Colloquium was a pivotal point in the history of Invest in ME Research as it celebrated its 10th year as a charity. Because, coming from the meeting, one detected a palpable sense of research into ME really having become an international concern – endorsing Invest in ME Research's strategy of international collaboration in research into ME.

Collaboration and working together can easily become just buzzwords – meaningless terms given out in press releases and handouts, attempting to make an impression that something is happening.

Yet BRMEC6, and the following public IIMEC11 conference, really did validate our long held belief that international collaboration in biomedical research can lead to patients being given back their lives.

We are hoping that BRMEC7 this year will produce a similar result. Last year was the first time that the Invest in ME Research conferences had a speaker from a government organisation.

It was wonderful to have Dr Vicky Whittemore representing the National Institute of Health, opening both our BRMEC7 Colloquium and IIMEC12 Conference and showing NIH visibility for this disease, and endorsing this international collaboration as a critical means to an end.

This year we are honoured also to welcome Dr Elizabeth R. Unger from the USA Centres for Disease Control. Dr Unger will be opening the Biomedical Research into ME 7 Colloquium 7.

Also attending will be the Norwegian Health Council – appearing at both Colloquium and

Conference – symbolising the huge potential and hope coming from the efforts of dedicated Norwegian biomedical researchers.

Both the Colloquium and Conference are high quality, forward-looking events that serve to improve knowledge of this disease, generate, and improve international collaboration into ME.

A high quality, professionally produced DVD of the conference proceedings will be produced as always – not a small task for a small charity – but it continues to serve not just as a historical record but also a means to educate doctors and clinicians about the seriousness of this disease. The DVDs have been distributed to twenty countries proving the increasing interest in research into this disease.

We were pleased to see that the US NIH listed as its goals for ME research the following -

- Advance research on the cause, prevention, diagnosis, pathophysiology and treatment of ME/CFS
- Encourage biomedical research investigators and organizations to study ME/CFS
- Communicate ME/CFS research information among and between NIH Institutes and Centres, and the NIH Office of the Director

The first two goals are similar to those that Invest in ME Research have been promoting and implementing for the past eleven years and have mentioned in our letters to the UK MRC, Department of Health and others in the position of influence.

The third has elements that epitomise the IIMER strategy as our proposal for a Centre of Excellence for ME – something we have been aiming for since 2010 – now develops.

Progress has inevitably been too slow from the patients' perspective but as we pass into our twelfth year as a charity, more and more signs and developments are indicating that things are changing.

Research into ME has needed a strategy – it was

surely missing when IIMER was formed and has continued to elude the major UK funding organisations.

Yet the Invest in ME Research strategy of bringing in researchers from other fields to help and improve biomedical research into ME was a necessity. It has been successful and well worth the effort and cost and we can witness this approach becoming more popular.

Our conferences bring together patients, researchers, clinicians and healthcare staff and allow knowledge and experiences to be shared – and IIMEC11 and BRMEC7 will see us entering our twelfth year in doing this. We will see many new faces in London as well as old friends.

Back to the theme of collaboration and high-quality research with a purpose.

Let us remember again these words that illustrate the Invest in ME Research approach to research into ME and the raising of awareness -

*"Vision without action is merely a dream.
Action without vision just passes the time.
Vision with action can change the world."*

Precisely the ethos of the Invest in ME Research Biomedical Research Colloquiums and Conferences!

Welcome to London - Welcome to IIMEC12 and BRMEC7

Kathleen McCall

CHAIRMAN INVEST IN ME RESEARCH



Biomedical Research into ME Colloquium 7

In 2011, Invest in ME Research initiated a different type of meeting that was appended to our annual public conference.

We gave that meeting the term "Corridor Conference" – as most of the productive discussions at seminars often took place in corridors or places away from the presentations.

And so the idea of the Biomedical Research into ME Colloquium was born. A meeting that would not compromise our research ethos with false views of ME but would instead concentrate on high-quality biomedical research and international collaboration.

"Coming together is a beginning;

keeping together is progress;

working together is success"

Invest in ME Research

BIOMEDICAL RESEARCH into ME

Building a Future for Research into ME

The Corridor Conference organised in London by liMER was followed with the impressive and forward-thinking collaboration with the Alison Hunter Memorial Foundation of Australia to form BRMEC2 – the two-day Clinical Autoimmunity Working Group (CAWG) research group which met in London the next year and before the IIMEC7 conference. This became our way of making rapid progress in biomedical research into ME. We attract experts from other disciplines to bring their expertise and skills to bear on this disease.

By doing this we can bypass the negativity and misinformation that has pervaded the perception of ME for a generation and influenced the establishment research bodies – and instead focus on proper science.

The **Invest in ME Research** Biomedical Research into ME Colloquiums are research meetings organised by the charity to encourage biomedical research into ME and international collaboration amongst researchers.

This is one of the main objectives of the charity. Invest in ME Research began arranging biomedical research conferences in our first year and have continued them ever since - mostly funded by the charity but with help from some wonderful supporters and some good friends.

The Invest in ME Research International Biomedical Research into ME Colloquiums began as a way of bringing together researchers from around the world in a round-table discussion of ME research and ideas. They are designed to encourage collaboration and sharing of experience and to bring in new ideas and knowledge from outside the field of ME. A small charity with a BIG cause can

COLLOQUIUM

achieve this.

Over the years this has broadened into sharing of experiences, data and plans for future research.

A culmination of much of this effort was the initiative to bring European researchers together to form **The European ME Research Group (EMERG)** which had an inaugural meeting in October 2015 in London to set up a strategy of European collaboration in ME research.

There is a basis now for creating a strategy of high-quality international biomedical research - something that has been lacking in the past. This will hold great promise of finding funding opportunities and raising awareness of biomedical research into ME.

As stated, our aim with the annual **CPD-accredited** research colloquiums has also been to introduce new researchers into the field of ME research, to gain new insights into the disease and enhance the strategy of research we are building.

The Invest in ME Research colloquiums have spawned a number of positive initiatives over the years and are the most successful research meetings for forming new research initiatives for ME with multiple collaborative initiatives being formed across continents.

We have proven that high-quality biomedical research can be initiated in an international, collaborative environment and we salute all those researchers who continue to participate and work with us for the benefit of all people with ME and their families.

We will continue to work together to facilitate the best hopes to make progress in finding the cause(s) of and treatments for this disease.

UK CENTRE of EXCELLENCE for ME

FAST TRACKING SOLUTIONS FOR ME

6eNTre
of Excellence for ME
investinmeresearch.org

Let's 6 It!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. UK Charity Invest in ME - Research (IMER) are establishing a Centre of Excellence for ME - a hub for research activity in Europe - enabling a strategy of high-quality biomedical research projects to follow, coordinated and collaborating with other institutes. Please support our C of E for ME. Let's Do It for ME. Let's C research into ME. See - <http://www.investinme.org/research.htm> #CofEforME #LetsCit @LetsDolt4ME

Invest in ME - Research (UK charity nr. 1153730)
www.investinme.org email: info@investinme.org

To create a base of research into ME has been the ambition of Invest in ME Research since 2007 – with more specific focus from 2010.

With the objective of improving and promoting education about ME amongst healthcare staff and raising awareness of the disease, the charity feels that the best way to make progress is to establish a national centre of excellence for ME.

To this end we have focused on facilitating research and resources to build the foundations of a UK Centre of Excellence for Biomedical Research into ME.

The charity believed that a change needed to be made in the way service provision for ME patients was carried out and proposed a simple but effective structure for providing services and instituting major biomedical research into this disease. This would have profound effects on the way ME is treated in the UK and establish a hub of scientific and clinical excellence for ME within Europe.

In the last years real progress has been made in achieving this and the charity has created and facilitated opportunities that can now boast five PhDs involved in research, with another planned to join in 2017 and a post-doc/research assistant being employed to facilitate a UK clinical trial of rituximab.

All of this is combined with national and international collaboration that is ongoing.

This substantial effort is, even if we say it ourselves, a tremendous achievement by our supporters and a validation of their commitment and support for this new way forward.

With our planned research ongoing and developing then we hope this will soon be possible.

Diagnostic tests and medical treatments can only be developed from sound scientific biomedical research. This is why the charity has concentrated much effort on establishing the research centre.

A clinical lead consultant would assess and plan the development of future services in conjunction with commissioning CCGs

It would provide access to specialist assessment, diagnosis and advice on

www.investinme.org

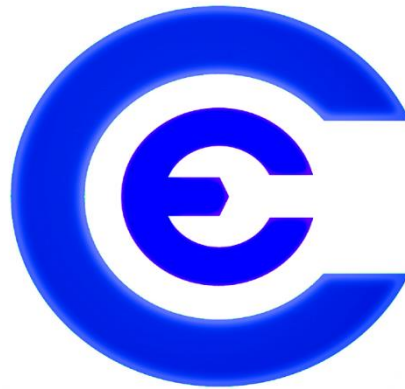
the clinical management, including symptom control and specific interventions, for both patients and health professionals.

The charity has held discussions with the Norfolk and Norwich University Hospital CEO and UEA Medical School to create a position for a consultant who can oversee proper examinations of ME patients which include diagnosis according to correct criteria and possibilities for acceptance into clinical trials being performed at the Centre, or in associated spokes of collaborative research.

There are also a number of new ideas being developed. Establishing a Centre of Excellence allows new ideas to be generated and more synergy to be obtained between different research disciplines. The research proposal would build a strategy of research that would involve patients, clinicians and researchers working together.

This will take a substantial effort to achieve but we feel it can be done and the rewards for people with ME would be huge. The Centre of Excellence for ME would be welcome news for patients, and their families and doctors, across Europe and would facilitate and initiate new international collaborations, consolidate and improve existing ones, and develop new research ideas. Funding bids would enable cooperation and sharing with joint projects being undertaken.

investinme.org



#CofEforME



The Centre of Excellence will also provide a high-quality partner for those Centres of Excellence being set up or existing in USA and Australia.

The Centre of Excellence for ME is not just one building or one lab – it is a model that has fundamental components of collaboration, data sharing and cooperation – sharing facilities, data and ideas.

With the help of leading researchers, the charity is proposing a number of initial projects that would help establish a research base and lead to further projects being initiated based on findings.



The research is the key component for change. Based on a strategy of biomedical research the Centre would create projects that dovetail and would collaborate with other centres where biomedical research into ME was taking place.

Apart from those researchers in the Norwich Research Park, the charity has also funded the B-cell research underway at UCL in London where Fane Mensah has been working under supervision of Dr Jo Cambridge.

The good relationship that has been established with the researchers at Haukeland University Hospital in Bergen continued and Dr Cambridge and Dr Fluge met in Stockholm at a conference organised by our European ME Alliance colleagues at RME Sweden.

This collaboration between high quality biomedical researchers - one of the major themes behind Invest in ME Research's research strategy - has been a great success with the Norwegians expressing to us, and Dr Cambridge, their

gratitude for the specialised knowledge and input that has been provided.

The UCL team are in the regular multi-centre status meetings in Bergen - such is the respect in which they are held, as well as continuing the good collaboration.

As we prepare for the UK rituximab trial this is good news indeed. It has now developed into closer collaboration with Dr Fluge and his team [visiting Norwich Research Park](#) in January of this year to discuss the UK rituximab trial and collaboration with the UK researchers on developing the best options for the UK rituximab clinical trial.

The Norwegian team will visit again in the autumn as the Phase III trial in Norway begins to establish results.

Having shown great vision and determination in looking at other areas of research linked to their phase III trial experiences and developing an incremental, evolutionary method of research then we feel the Norwegian Haukeland researchers have exactly the model of how good research should proceed.

Establishing such a Centre represents a very progressive step in looking for cause(s) of ME and the possibilities will be further increased as the research team moves into the new Quadram Institute, which will open next year.

More information is on our microsite at <http://www.cofeforme.eu> where there are ways to help us raise funds and awareness of this venture - see <http://www.investinme.org/ce-Support-cofeforme.shtml>

Our hashtags for the Centre are **#CofEforME** and **#LetsCresearch**.

The Centre of Excellence will also provide a high-quality partner for those Centres of Excellence being set up or existing in USA and Australia.

The Centre of Excellence harnesses the benefits of

collaborative biomedical research in modern facilities with world-class researchers. Our aim is to establish a sustainable examination and research centre that would form the hub of European research and treatment for this disease and produce a pathway to produce huge benefits for the nation, and further across the world.

We invite all to support us as we move forward with research. Let us make this vision a reality.
<http://investinme.org/ce-thecentreforme.shtml>

Quadram Institute Bioscience

The Institute of Food Research (IFR) and Norwich Medical School will relocate to the new Quadram Institute building that is set for completion in 2018.

One can follow the QI progress at this link in Norwich Research Park here -
<https://quadram.ac.uk/>

As a first step to realising the ambition of the Quadram Institute, on April 28 2017, the Institute of Food Research (IFR) transformed into Quadram Institute Bioscience.

The lead of the Quadram Institute is Professor Ian Charles – who is again giving the keynote speech at the Invest in ME Research IIMEC12 international Conference.



Professor Charles opened IIMEC10 - the 10th Invest in ME Research

International Conference in London in 2015.

He has over 30 years' experience in academic and commercial research and was a founding member of The Wolfson Institute for Biomedical Research at University College London, one the UK's first institutes of translational medicine. More from Quadram -

https://quadram.ac.uk/research_areas/gut-microbes-health/

Norwich to be Home to the Quadram Institute

The Quadram Institute is located on the Norwich Research Park and will integrate under one roof research teams from the current Institute of Food Research (IFR) and University of East Anglia's (UEA) Faculty of Science and Norwich Medical School with the Norfolk and Norwich University Hospital's (NNUH) gastrointestinal endoscopy facility.

OUR CURRENT FUNDING STREAMS



Centre of Excellence
18.1% of £1670k
for ME

The UK Centre of Excellence for ME

Support for the UK Centre of Excellence for ME will provide a solid foundation for high-quality biomedical research into ME. This approach to research will change the landscape for research into ME and make this an area of research that will encourage innovation and novel research.



B-cell/Ritux
98.46% of £520k
Trial

Rituximab Trial/B-Cell Research

The B-cell/Rituximab research. The charity is keen to replicate the recent Norwegian findings using Rituximab. We initiated B-cell research at UCL leading to a UK rituximab clinical trial.

A specific web site has been set up to document this project – see www.ukrituximabtrial.org.



Gut Microbiota
94% of £200k

Gut Microbiota Related Projects

Beginning with our foundation project at Norwich Research Park. It is not often realised that 60-70% of the immune system is located in the gut as a vast network of lymph tissue referred to as GALT (gut associated lymphatic tissue). The research highlighted in the proposal involves looking at gut microbiota, which is some of the latest thinking in how to go about research. A foundation project at the University of East Anglia began in 2013 - funded by the charity.



Medical
10% of £59k
Students

Medical Students

Part of the charity's strategy for improving education has been to involve medical students in research into ME. By participating in the research projects funded by the charity then students are able to learn far more about ME and patients as well as passing on the reality of this disease to their peers.

THE Big Give for the BIG Cause Project

We welcome investment in developing the UK Centre of Excellence for ME and support from all who wish to see research into ME based on high-quality science and an urgency in all efforts to tackle this disease.

Invest in ME Research have a Big Give page describing the basics of establishing a Centre of Excellence for ME and a donate option for supporting this work.

The link is here <https://secure.thebiggive.org.uk/projects/view/9169>



Join our C Selfie Campaign to Raise Awareness

To support the UK Centre of Excellence for ME we are asking people to send in photographs - or ask your MP, GP, any celebrities, sportspeople, etc. to support the campaign.

To show support please take a photo of the person supporting us by using the right hand and make the C sign for supporting the charity's proposal for a Centre of Excellence for ME.

Just send the photos to Invest in ME Research (our e-mail address is cofeforme@investinme.org) and include some short information or story behind the photograph



[#COFEFORME](#)

[#LETSCRESEARCH](#)



Finding, Facilitating, Funding Research into ME

Part of the development of the UK Centre of Excellence for ME consists of involving medical students in the research by intercalating in their fourth year of medical studies, and facilitating and encouraging students to look for a career in researching ME.

An example recently demonstrate the benefits in our strategy of having medical students involved in research into ME.

Navena Navaneetharaja and Verity Griffiths have been involved in the gut microbiota research in Norwich Research Park. Navena also spent several months with Professor Maureen Hanson at Cornell University in New York, USA. They produced a paper together with Professors Wileman and Carding from the Centre that provides a comprehensive review of the current evidence supporting an infectious aetiology for ME/CFS. This led the authors to propose the novel concept that the intestinal microbiota and in particular members of the virome are a source of the “infectious” “trigger of the disease. Such an approach has the potential to identify disease biomarkers and influence therapeutics. The paper is -

A Role for the Intestinal Microbiota and Virome in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)?

Abstract from the Paper

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a heterogeneous disorder of significant societal impact that is proposed to involve both host and environmentally derived aetiologies that may be autoimmune in nature. Immune-related symptoms of at least moderate severity persisting for prolonged periods of time are common in ME/CFS patients and B cell depletion therapy is of significant therapeutic benefit. The origin of these symptoms and whether it is infectious or inflammatory in nature is not clear, with seeking evidence of acute or chronic virus

infections contributing to the induction of autoimmune processes in ME/CFS being an area of recent interest. This article provides a comprehensive review of the current evidence supporting an infectious aetiology for ME/CFS leading us to propose the novel concept that the intestinal microbiota and in particular members of the virome are a source of the “infectious” trigger of the disease. Such an approach has the potential to identify disease biomarkers and influence therapeutics, providing much-needed approaches in preventing and managing a disease desperately in need of confronting.



<http://www.mdpi.com/2077-0383/5/6/55>

Another paper produced from IIMER funded research at UCL was released recently. Fane Mensah produced a paper with Dr Amolak Bansal, Brian Ford and Dr Jo Cambridge

Chronic fatigue syndrome and the immune system: Where are we now?

Abstract from the Paper

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is characterised by multiple symptoms including fatigue, headaches and cognitive impairment, which have a significantly adverse effect on the normal functioning and well-being of the individual. These symptoms are often triggered or worsened following physical or mental exertion. ME/CFS has long been thought of as having a significant immunological component, but reports describing changes in immune function are often inconsistent between study groups. Although the wide range of physical, neurocognitive and autonomic symptoms reported have seriously hampered attempts to understand pathophysiological pathways, investment in

biomedical research in ME/CFS is finally increasing with a number of novel and promising investigations being published. The onset of ME/CFS may often be linked to (viral) infections which would be consistent with a variety of alterations in natural killer (NK) cell function as described by a number of different groups. Consistency in cytokine data has been lacking so far, although recently more sophisticated approaches have led to more robust data from large patient cohorts. New hope has also been given to sufferers with the possibility

that therapies that deplete B cells can result in clinical improvement. To understand the pathogenic mechanism in this complex condition, it is important to consider repeated analysis in different cohorts. In this review, we will discuss the potential of different components of the immune system to be involved in the pathogenesis of ME/CFS.

<https://www.ncbi.nlm.nih.gov/pubmed/28410877>

“My beautiful daughter is totally bedbound. She has a diversity of symptoms that seem endless. (Most of the very severely affected have between 60+ and 100+ symptoms). The worst thing of all is the relentless, agonising pain. Widespread pain in every muscle, joint, and organ possible.



She has not had one day free from pain since the illness began.

Her whole life now is lived from her bed. Not her choice for she is a talented artist and photographer and she dreams of being in summer meadows photographing the dancing bees and butterflies and painting the colourful flowers.

“Her dreams have been snatched from her by this awful disease that others misunderstand by thinking it's just about feeling tired or attention-seeking”....

“Her days are spent in a darkened room and in as much silence as the outside environment will allow. She is hypersensitive to light, noise, odour, vibration, touch, movement, chemicals, some foodstuffs, and medicinal drugs.”

“She is unable to sit or stand due to being moribund with pain, orthostatic intolerance, paralysis, blackouts and much more and so her bed is her companion twenty-four hours a day. She cannot tolerate touch as her skin is always 'on fire' like it's been grated with a cheese grater. Her description. I have to cut her pyjama tops off (when she can tolerate a change of tops) because any movement causes her indescribable pain. She has difficulty speaking sometimes and so asks me to be her voice..... “

” My amazing daughter has such a positive view of life.

I'm stunned that she's not depressed or angry.

Although she sometimes has her low days, her courage and inner strength are immeasurable. Not a day passes without seeing one of her magical smiles which sometimes just breaks my heart.”

- from Lili <http://investinme.org/mestory1010.shtml>

RESEARCH – COLLABORATION

Research News from Fane Mensah

Fane Mensah is funded by Invest in ME Research for B-cell research [**The potential role of B cells and their products in ME/CFS Patients**]

Collaboration with Christopher Armstrong

As part of our Solve ME/CFS Initiative Ramsay award winning collaboration, Christopher Armstrong from the Bio21 Institute (Melbourne University, Australia) came over to work with us at UCL for one month.

A quick flashback to June 2016, at the 6th Invest in ME Research International Biomedical Research into ME Colloquium (#BRMEC6) meeting in London where Chris and I met. We were the two youngest scientists at the meeting to give a presentation about our research.

It would not have been the first thing we would have in common!

Straight after our presentations we started to talk about each other's experiments and found out that the two completely different fields we were working in (Immunology and Metabolomics) could be complementary.

It is well known that immune issues have often been associated with ME/CFS (B cells, NK cells T cells etc.).

More recently, different groups, including Christopher and his colleagues have studied changes in the metabolic profile in ME/CFS patients.

Their data is very promising and consistent which supports a possible role in this condition.

Following some bonding drinks after the conference, Christopher visited us (myself and Dr. Cambridge) the next week at UCL where we laid the base for our collaboration.

After Christopher returned to Australia, and several (late and early) Skype meetings we put together a grant application for the Solve ME/CFS



Initiative Ramsay award which is an award that supports (young) scientists from different fields committed to ME/CFS research. This award gives them the opportunity to lay the basis for more substantial collaborative research projects.

The next generation scientists: BSc student internship at UCL

With the support of the Invest in ME Research charity, we were very fortunate to have Isabelle de Rooij visiting our laboratory for a 5-month internship. Isabelle is a BSc student from Hogeschool Rotterdam in the Netherlands (my old University) undertaking the Bachelor of Science course in biology and medical laboratory sciences. As tipped for the best student in her year, we had big expectations from here and she did not disappoint us!

During her internship, she not only learned

different laboratory skills and techniques but also got an insight into the biomedical research applied to ME/CFS. This was just as important as the technical part of the internship.

Isabelle really enjoyed her time her and was very

The article by Fane shows the importance of Invest in ME Research's strategy of international collaboration in research into ME.

The meeting between Fane and Chris (and Zaher Nahle from Solve ME/CFS) came about because the charity invited all of them to the **#BRMEC6 Colloquium**.

The article also demonstrates the importance of our strategy of funding students in research into ME - a strategy proven to be successful and making a real difference.



passionate about her project. She significantly contributed to the development of new protocols for our future experiments, and assisted me with ongoing projects related to the joint project with Christopher Armstrong.

We were very proud of Isabelle when she finished her internship, which was examined based on her technical lab skills and final report, with 9.5/10.

A great achievement from a great student! Her university was so impressed and satisfied with her achievements and progress in our group that they have asked us if we would be interested in future collaborations.

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ME QUOTES

"It is of the greatest importance to keep in mind the goal toward which one works in science, but it is also of equal importance to simply explore and define the 'new' while keeping that mind well prepared for finding new treasures. It is only through such efforts that we believe the etiology of CFS will be finally illuminated."

*Steven Tracy and Nora Chapman,
University of Nebraska Medical Center:*

<http://www.investinme.org/ArticleJ31-Human Enteroviruses and Chronic Infectious Disease.shtml>

From Invest in ME Research



SCIENCE,
POLITICS,

.....

and ME

At the 10th Invest in ME Research International ME Conference in 2015 Dr Ian Gibson announced that he was planning on writing a book about ME - and the politics and prejudice which has affected the way that ME is perceived, treated, researched and funded - as well as the resultant effects on patients and their families.

Dr Ian Gibson led an inquiry into ME in 2006 [2]. Without official funding, and at a time when unbiased and independent analysis on the way ME was being treated and reported on by the establishment organisations and media was lacking, Dr Gibson provided a checkpoint which attempted to get publicity and force change which would help ME patients.

The Inquiry's report made several recommendations [3].

That the then Labour government ignored the report, and its recommendations, will forever cast a shadow on the health minister at the time and on the government itself.

Since that time Dr Gibson has been influential in assisting IIMER get high-quality biomedical research established in Europe.

He has also chaired the IIMEC* conferences.

After 12 years of IIMEC* conferences, and following the tenth anniversary of the Gibson Inquiry, and when change was slowly managing to creep into establishment organisations, Dr



Gibson felt it was necessary to look at the way that politics and the actions of some have influenced the way ME has been, and



continues to be the subject of misrepresentation, inappropriate media reporting, ineffective research funding and a pervading prejudice that needs to be exposed.

Dr Gibson is familiar with the political events in the UK, how they affect healthcare and patients and how some organisations and individuals are unduly influencing these policies.

It is important to understand the politics of ME and how the 'establishment' in most countries reacts.

Dr Gibson, and co-author Elaine Sherriffs, started interviews with knowledgeable individuals following the IIMER London conference and established new contacts. Dr Gibson and Elaine visited or interviewed researchers, clinicians, advocates, patients, carers and others to produce this an analysis of ME - the Science and Politics behind the way ME is treated.

Although heavily constrained by the limited funds that the charity was able to raise interviews were carried out by Elaine and Dr Gibson – and included a visit to Stockholm, Sweden, where they spoke with patients, clinicians, researchers and politicians from Sweden and other countries.

The project was aided by a generous donation

toward the production of the book from the **Irish ME Trust**. We also had donations from some individuals for which we were extremely grateful.

The book was published earlier this year and is available via Amazon.



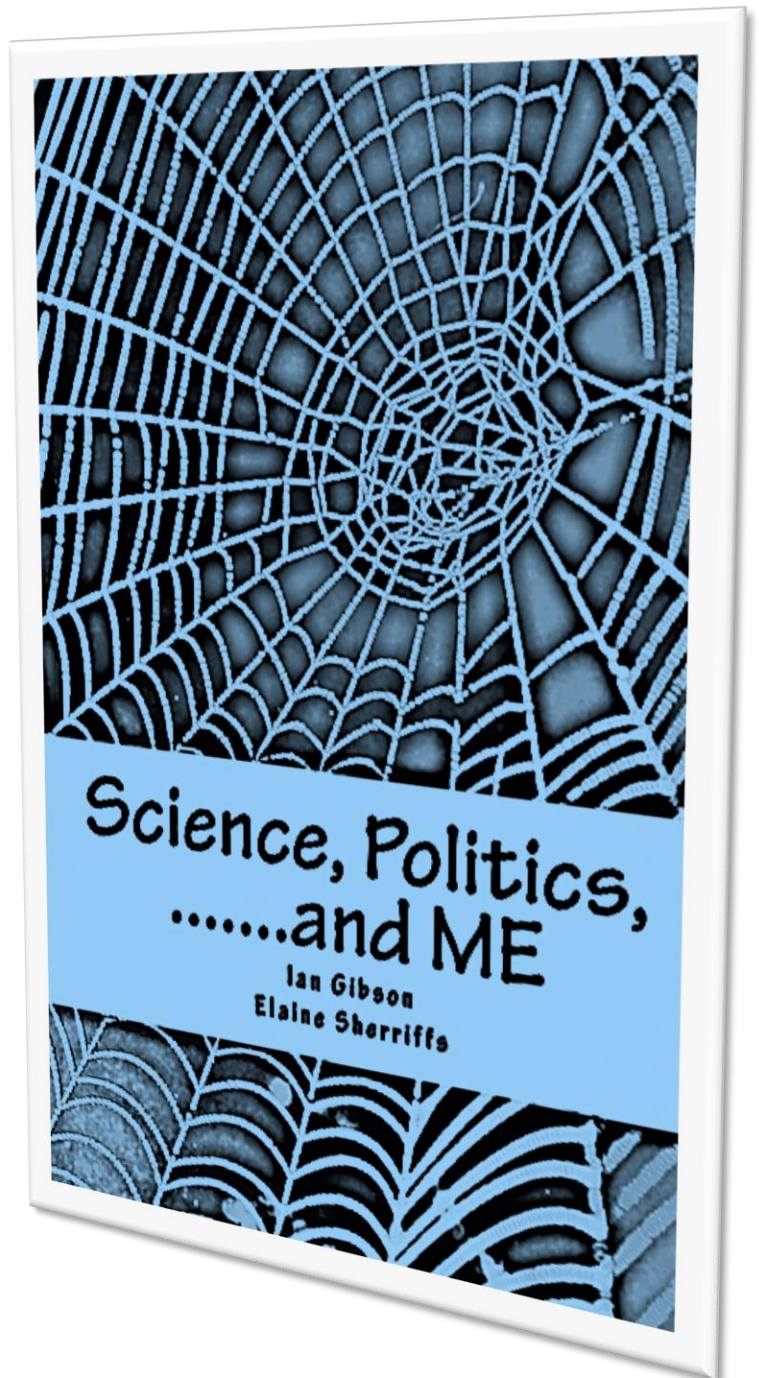
Few diseases can have been so maligned by false information, so manipulated by an insidious establishment-controlled ideology, or so poorly dealt with by those holding the purse strings for research into the disease, than Myalgic Encephalomyelitis (ME).

This book examines a scandal in our generation - a scandal still being played out by corrupt, apathetic, inept or ignorant attitudes in governments and Medical Research Councils and health services.

We welcome all support for raising awareness of the book – a book able to reach more people in society in a way that should make them want to know more and question why a section of the population are being so abused by crass, self-serving and

Please help in raising awareness of this book. Thank you for your support.

[Buy from Amazon](#)



References:

- 1 [IIMEC10 10th International ME Conference](#)
- 2 [Gibson Inquiry Report 2006](#)
- 3 [Gibson Inquiry Recommendations](#)
- 4 [Gibson Book - JustGiving Donations](#)
- 5 [Gibson Book - The BIG Give Project](#)

Philanthropy and ME

Philanthropy – *“the desire to promote the welfare of others, expressed especially by the generous donation of money to good causes”*

Philanthropists may be thought of as wealthy, individuals or organisations contributing to causes, for reasons either personal or financial or from expediency.

But philanthropy comes in all flavours and different guises and not always from obvious quarters, and not always by means of donating money.

The philanthropy given and displayed by supporters of Invest in ME Research is of the highest level. Many of the charity’s supporters are very ill and have little means of financially contributing – left with little financial possibilities due to the ravages of the disease on them or their family, exacerbated by punitive and immoral government policies on welfare benefits to disabled people.

Yet their efforts made to support the charity and its research has changed the landscape of UK research into this disease – forcing biomedical research into the mainstream when, for years, little was done to make progress by existing establishment organisations.

LDIFME

The Let’s Do It for ME (LDIFME) campaign and our core group of supporters are helping to fashion a change in ME research and this determination and enthusiasm will influence researchers – both within the ME research area and those from outside.

As the charity initiated a plan to develop a Centre of Excellence for ME an idea was born by



Jo Best and helped on by Jan Laverick and Paul Kayes – all ME patients. Instead of continually reacting to what others were doing or saying they decided to take a proactive approach. A campaign was started to support the Invest in ME Research proposal for the Centre of Excellence for ME.

The difference with this campaign? To use the skills and ideas of patients who want more than anything else does to regain their health.

By harnessing these ideas and enabling people to feel positive about doing something themselves to effect change then the campaign could be turned into something which was fun.

Positive campaigning – with an objective to fund sorely needed translational biomedical research into ME and to harness patient power to influence ME research – something which had been missing from the equation.

The Let's Do It For ME campaign is a positive and proactive campaign. The aim is to raise funds for

biomedical research but everyone's input is welcomed - be it just ideas or moral support for other people's fundraising.

Whilst raising funds for biomedical research the campaign has also raised much needed awareness and this has allowed more correct information about ME to be disseminated.

Let's do it for ME! is a patient-driven campaign to raise awareness and vital funds for the [UK Centre of Excellence for ME](#) performing translational biomedical ME research, clinical assessment, diagnosis and treatment for patients, and training and information for healthcare staff based at the Norwich Research Park in the UK but working collaboratively with international biomedical researchers.

The Let's Do It For ME campaign has been running now for 7 years.

<http://ldifme.org>

Invest in ME Rituximab Research Fund
www.ukrituximabtrial.org
On
#InternationalMEAwarenessDay

£512,000
Target = £520,000
Invest in ME Research - Let's Do It!

“We constantly receive letters from the Department of Health stating that very little is known about ME and yet without doctors like Dr (Nigel) Speight, who are willing to believe in and listen to children with ME and learn in the process, many patients would have little hope for a better and safe future. Paediatricians and doctors in the UK generally demonstrate an overwhelming degree of ignorance toward ME– either disbelieving it exists, misdiagnosing other diseases in its place, failing to identify the potential consequences of severe ME and failing to spend any time in improving their education about the disease. Sometimes they just continue to hold their pet theories on this disease.

The Institutes of Medicine concluded in their report of 2015 [9] that ME is an organic disease.

The IOM report looked at the effects on children from this disease [10]. “There is clear evidence of the impact of ME/CFS on the education and social development of these young people. The stigma and social effects of paediatric ME/CFS include the loss of normal childhood activities and in some extreme instances, inappropriate forcible separation of children from their parents”

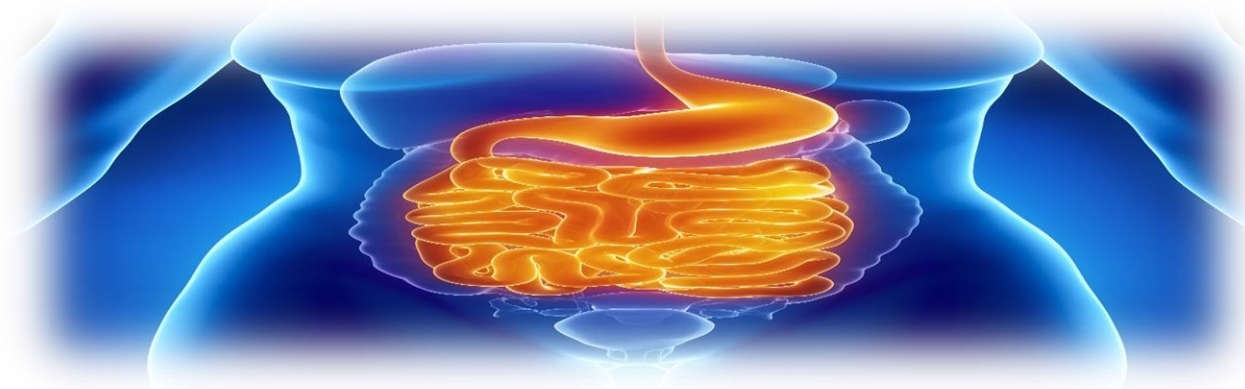
As part of the research review carried out the IOM reported on an Australian study of 189 adolescents by Rowe and Rowe concluded that evidence for somatization disorder among young people with ME/CFS was negligible. “They all note that ME/CFS symptoms often make it more difficult to do schoolwork, so children and adolescents with ME/CFS may be misclassified as having “school phobia.”

Invest in ME Research deplore the concocted term school phobia, or pervasive refusal syndrome, and those promoting these terms in relation to ME/CFS, as they have never applied to children with this disease.”

Invest in ME Research - Ignoring the Elephant in the Room

<http://www.investinme.org/IIME-Newslet-1604-NS999.shtml>

The gut microbiome in Myalgic Encephalomyelitis



Maureen R. Hanson and Ludovic Giloteaux
(Cornell University, USA)
April 2017 © Biochemical Society

Over the last dozen years, increasingly powerful DNA sequencing methods have allowed characterization of the microbes residing on and in humans in much greater detail than ever possible

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<http://www.biochemistry.org/>

before. Abnormalities present in the gut microbiome—those microbial communities residing in our intestines—have now been observed in a number of diseases. One such illness is Myalgic Encephalomyelitis (ME), also known as Chronic Fatigue Syndrome (CFS).

CFS was a name coined by the US Centers for Disease Control (CDC) in 1988, and reviled by patients for the resultant trivializing of this serious illness. Recently, the US National Academy of Medicine (NAM) recommended a new name: Systemic Exertion Intolerance Disease, though this name is not yet widely used. In ME, as in other diseases, the diversity of the bacterial species in the gut microbiome is lower than in healthy individuals. Furthermore, the abundances of different bacterial residents of the gut, which influence health both favourably and negatively, differ between ME patients and healthy controls. Bacteria translocate into the blood in greater amount in ME, leading to inflammation. Dysbiosis in the gut likely contributes to symptoms in this life-limiting disease .

Three to four times more women than men have ME. Children and adolescents as well as adults are susceptible to the disease. Prevalence is difficult to determine because of the lack of a simple, objective diagnostic test. While physicians experienced with the disease are readily able to make correct diagnoses, the clinical criteria often vary between studies, making enumeration of patients difficult. An investigation of ME in three regions of England found that about 0.2% fit a widely used 1994 CDC definition. A meta-analysis of 14 studies

found the prevalence by clinical assessment to be 0.76%. These numbers translate into 128,000 to 486,000 ME patients in the UK. Thus, even if the lower figure is used, ME does not fit the definition of a rare disease (see www.raredisease.org.uk). An example of a rare but serious disorder that affects intestinal function is *Clostridium difficile* infection which is at least 10 times less common than ME.

The severity of the disease varies, though most affected individuals are unable to work or attend

school full time. For example, a small survey of 25 children with ME in the UK found that only one could attend a full day. Indeed, another study found that ME was responsible for 42% of the medically certified, extended school absences in the UK over a five-year period.

While the 'fatigue' element in the name emphasizes a major symptom of ME, most patients report that the fatigue is not the same as that experienced by healthy individuals after vigorous physical exercise or inadequate sleep. Instead, the fatigue is described as a profound lack of energy, more akin to the sensation of exhaustion that occurs during a severe case of influenza or mononucleosis. Two additional symptoms were identified by the National Academies of Medicine committee in a 2015 report (<http://www.nationalacademies.org/hmd/Reports/2015/ME-ME.aspx>) as hallmarks of the disease: post-exertional malaise and unrefreshing sleep. The new diagnostic criteria also require either cognitive impairment or orthostatic intolerance. The latter refers to a surge of symptoms when upright that improves when the patient reclines, likely due to a disturbance in the autonomic nervous system. With regard to cognitive impairment, patients often report 'brain fog,' like the impaired mental capacity, poor memory and

concentration that healthy individuals experience when they have been awake all night.

Most people with ME reach a steady-state level of physical and/or mental activity they can sustain without inducing an ensuing increase in symptoms known as post-exertional malaise. Many are homebound – simple acts such as shopping for groceries can result in worsening of their symptoms. For those who are bedbound, any sort of stimulation, even the mental and physical effort to carry on a conversation, can intensify their symptoms. Many ME patients, whether bedbound or not, are unusually sensitive to light and sound. Bedbound patients often require eyeshades and sound-protecting headphones to cope with those stimuli. Among the most severely ill ME patients (Figure 1), some must be supported at the level of those who are comatose. Some are too impaired to speak and cannot eat nor digest food normally and must be tube fed.

Possible roles of the gut microbiome in ME

Gastrointestinal disturbance is a symptom often reported by ME patients. This fact has encouraged several investigators to compare the gut microbiome in patients versus controls.



Figure 1. ME devastates lives. A healthy college student one month before becoming ill with ME (left), soon becomes too debilitated to sit up, unable to tolerate light nor sound. Bedbound for two years, he becomes unable to chew and must enter hospital to receive a feeding tube because he is too weak to eat.

Our research group undertook a study of the bacterial gut microbiome by comparing 16S rRNA from faecal samples of 48 ME patients and 39 controls. The 16S rRNA sequence is commonly used to identify bacterial species, as the presence of very variable regions in

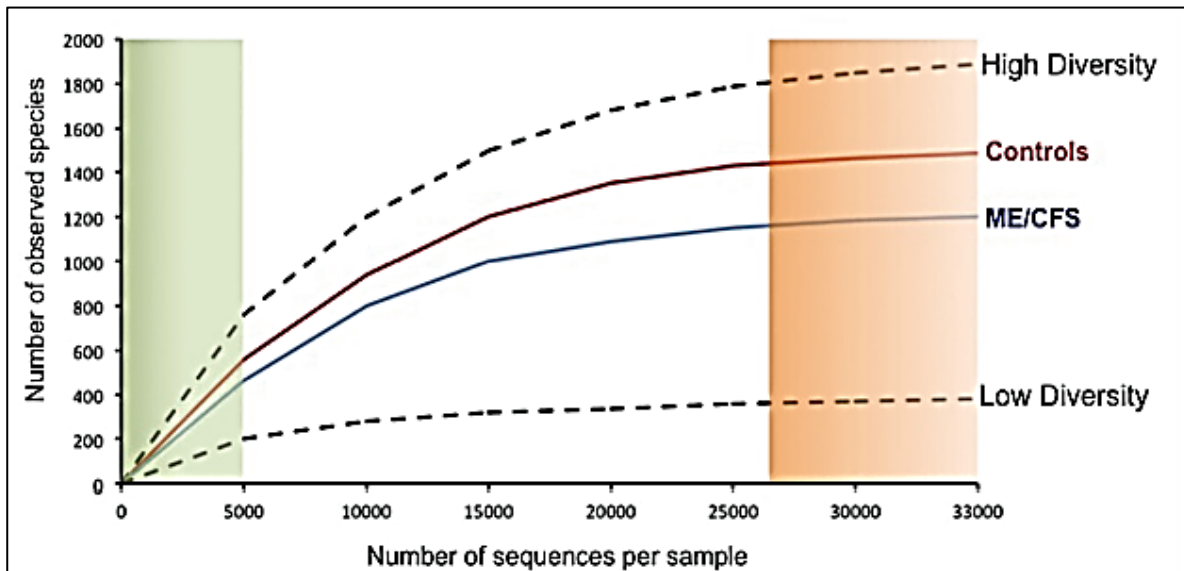


Figure 2. Rarefaction curve, graph of species detected per sample sequenced. When the slope is steep, many species remain to be discovered. At the plateau, most species have been detected and additional sequences will not reveal many more.

the 16S rRNA gene provides species-specific signature sequences. We obtained an average of 98,000 sequence reads per sample, more than ample to identify almost all of the bacterial diversity. To determine how many reads are needed, the number of species detected per number of sequences can be graphed to produce a 'rarefaction curve' (Figure 2). As more sequences are obtained, the number of species detected increases until a plateau is reached, where few additional species will be found

despite a large number of additional sequence reads. For our samples, it is evident that 30,000 reads would be more than sufficient. For the example shown of a theoretical sample with low diversity, 5000 reads would have been adequate, while the high-diversity example indicates that even 30,000 reads would not suffice.

A conclusion that can be drawn from Figure 2 is that ME cases have reduced bacterial diversity in comparison to healthy controls. Such reduced diversity has been observed in other diseases such

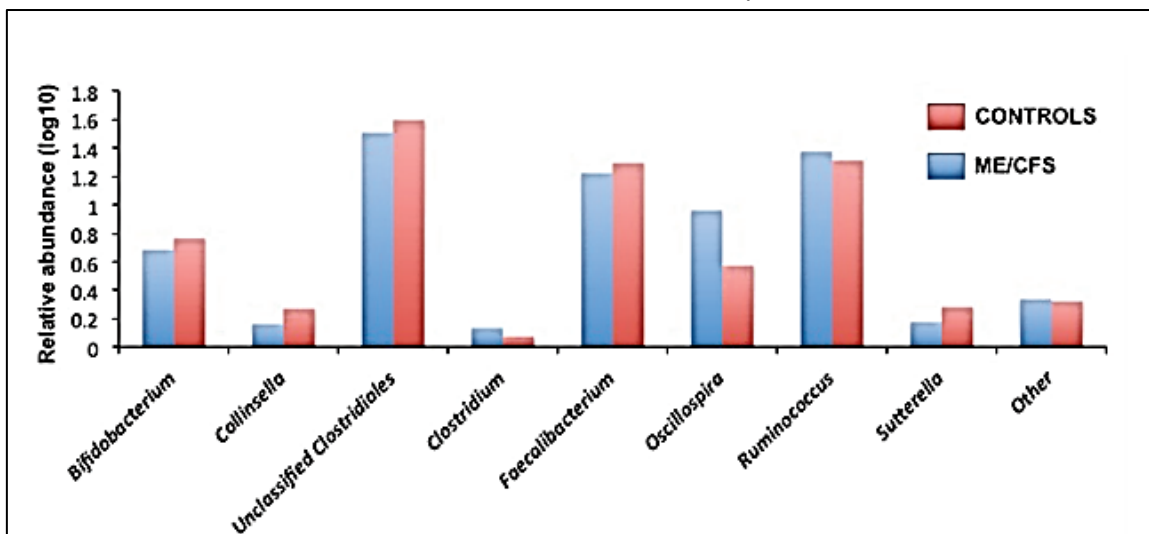


Figure 3. Differences between abundance of members of bacterial genera in ME patients versus healthy controls. A log10 scale is used in order to fit genera with large ranges of abundance onto the same graph. All differences shown are statistically significant ($p < 0.05$).

as *Clostridium difficile* infection, inflammatory bowel disease and necrotizing enterocolitis.

The sequence data can also be analyzed for differences in the abundance of various species between cases and controls. Some species that we found to be differentially abundant represented a very small fraction of the bacteria present and thus may not have a large effect on gut ecology and function. In Figure 3, we show those genera that a) represent more than 1% of the gut microbiome and 2) varied significantly among faecal samples between ME and healthy controls. The reduced abundances of *Bifidobacterium* and *Faecalibacterium* species in patients have also been reported in inflammatory bowel disease and other conditions. *Faecalibacterium* species produce butyrate, a short-chain fatty acid that has anti-inflammatory properties, and thus its reduction would predict lower levels of butyrate. While we did not measure butyrate in our samples, when faecal samples of 34 female cases and 25 controls were examined by Armstrong et al. in another study, surprisingly, butyrate was higher in the ME patient samples. Determining which metabolites are actually present in the gut can be difficult to predict merely from a list of species that reside there, given the complex interactions among different microbial communities and with the cells in the intestine.

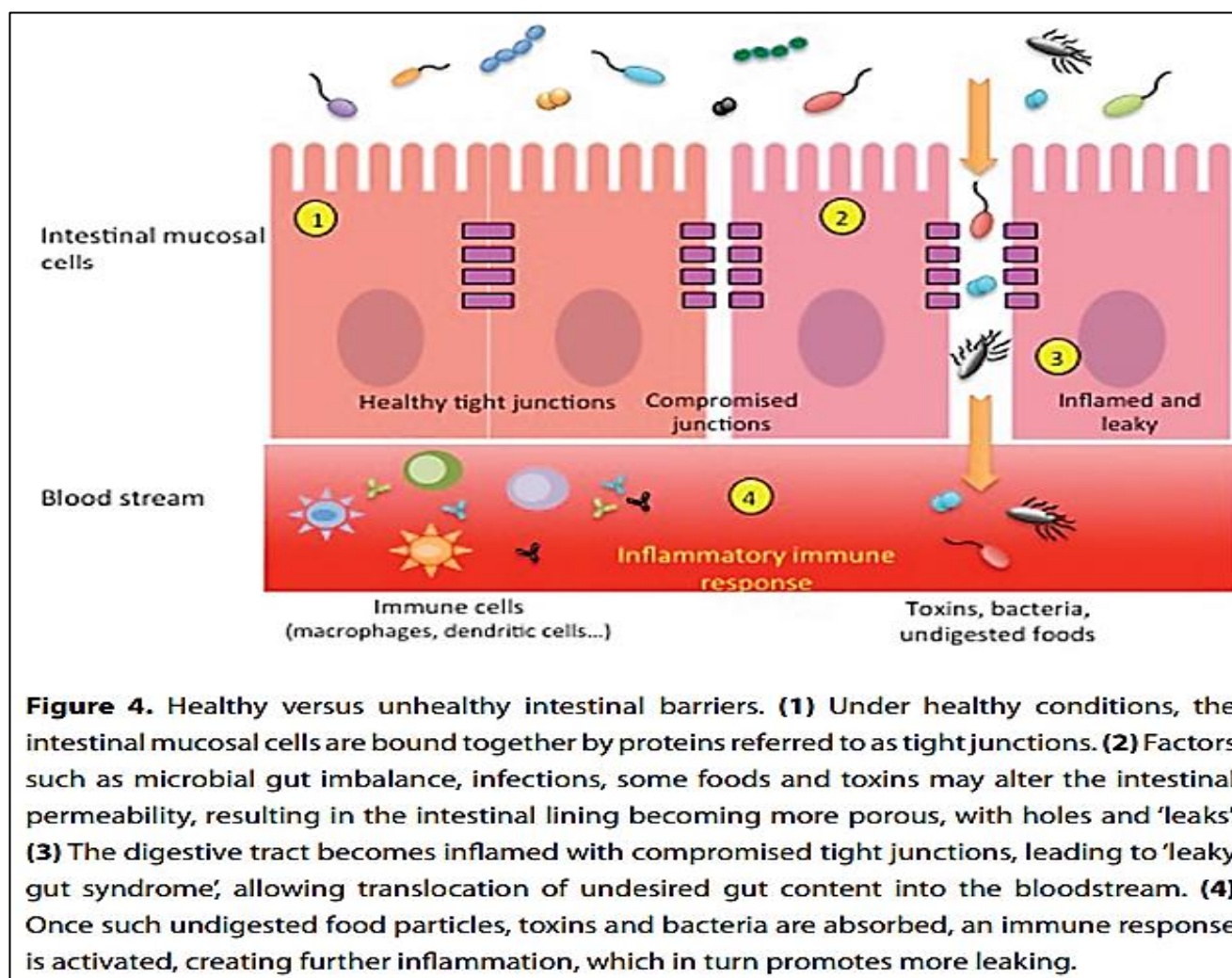
Several studies in which bacteria were cultured also demonstrated differences between ME patients and controls. However, many gut microbial residents cannot be cultured and are known only by their DNA sequences, so that high-throughput sequencing of 16S ribosomal DNA for identifying bacterial taxonomic groups is beginning to supplant culture methods. Nevertheless, there are also limitations to knowledge from DNA sequences of intestinal contents. For example, while ribosomal DNA sequencing can detect that *Escherichia coli* is present, it doesn't reveal whether one of the highly virulent *E. coli* strains is present in addition to benign or beneficial *E. coli* strains that reside in

most individuals. To find pathogenic *E. coli*, bacteria are grown on specific culture media and then tested with an antibody that reacts with proteins present in disease-causing *E. coli* strains. Thus, a harmful bacterium could be present in ME patients and go undetected by ribosomal DNA sequencing.

Leaky gut problems

When the intestinal lining is inflamed, bacteria can translocate into the bloodstream through loosened intestinal tight junctions leading to a 'leaky gut' (Figure 4). The immune system then detects the presence of bacteria or bacterial components in the blood and mounts an immune response to counter this apparent invasion. There can be collateral damage from the immune system's attack on perceived threats. ME patients often have symptoms of chronic inflammation such as muscle and joint pain and swollen lymph nodes.

In order to find out whether ME patients might have more bacterial products in their blood than healthy people and could be responding to them, we tested whether the levels of certain molecules were different in the blood of the same ME patients and healthy controls whose faecal samples were sequenced. We found that patients had higher levels of lipopolysaccharides (LPS), a large molecule comprised of both lipid and sugar components. LPS are present on the outer membrane of some bacteria and cause a strong immune response. We found that levels of LPS, LPS-binding proteins and a receptor for LPS-binding protein (soluble CD14), which signals the presence of LPS to the immune system, are increased in ME patients. Thus, the abnormal gut microbiome in ME patients likely contributes to their chronic inflammation and ensuing symptoms. While digestion most often comes to mind when considering intestinal bacterial species, there is increasing evidence that the gut microbiome affects the risk of colorectal cancer, obesity and abnormal mental function. Metabolites and proteins from the gut enter the bloodstream in healthy as well as diseased individuals, and some can affect the central



nervous system and brain.

Prospects for treatment

Oral prebiotics and probiotics are being investigated for restoration of bacterial diversity and resolution of gastrointestinal diseases. Prebiotics are substances thought to improve growth of beneficial species, while probiotic supplements contain microbes known to be present in healthy guts. In order to be incorporated into a probiotic pill, bacteria must be grown in culture, but culture conditions for growing many of the bacterial species present in the human gut are not known. Thus, only a selection of certain species can be incorporated into commercially available probiotics. How these different species affect people with different types of gut microbiomes, and whether gastrointestinal illnesses can be improved with their aid is an important topic that is currently being explored in the research community being explored in the research community.

Because pure cultures of many gut microbes cannot be obtained, researchers have turned to faecal transplants, i.e. introduction of faecal material from healthy human donors into recipients. This treatment has cured some individuals with severe gastrointestinal dysfunction from *Clostridium difficile* infection. Whether this process can also help patients with other types of intestinal diseases and ME is less clear. Promising reports have appeared about improvements in ulcerative colitis, Crohn's disease and autism. With regard to ME, anecdotal reports from patients who have tried faecal transplantation indicate some reduction in symptoms, but not complete recovery nor persistent improvement in their conditions. One study of faecal transplantation indicated that 42/60 ME patients had a favourable response. The results are sufficiently promising to suggest that a clinical trial of faecal transplants in ME would be worthwhile.

Future directions

Multiple studies now show that the gut bacterial composition is abnormal in patients with ME, a lifelimiting disease. These findings are now among many discoveries of biological differences between ME patients and healthy individuals, all of which should dispel any remaining notions that the illness is psychological in nature. Future studies on the

eukaryotic microbiome and virome may reveal additional disturbances in the microbial communities of people with the disease. While these gut abnormalities may be a response to some other inciting factor, rather than the basal cause of disease, learning how to ameliorate them could have clinical benefits for patients and help promote recovery, perhaps in conjunction with other treatments. ■

Ludovic Giloteaux

Ludovic Giloteaux, PhD, is a Research Associate in Dr Hanson's lab group. His research addresses the molecular mechanisms of biological processes, ranging from environmental concerns such as the bioremediation of arsenic- and uranium-contaminated environments to human disease, namely the biological basis of ME. His research uses integrated approaches combining molecular biology and microbiology to study the microbiome in ME, and the effect of the disease on gene expression and proteins from immune cells. Email: lg349@cornell.edu.



Maureen Hanson

Maureen Hanson, PhD, is Liberty Hyde Bailey Professor in the Department of Molecular Biology and Genetics at Cornell University in Ithaca, New York. Her research projects concern gene expression and genetic engineering in plants and the molecular basis of ME/CFS, funded at various times by NSF, USDA, DOE, NIH and several non-profit organizations. Her lab has produced over 180 peer-reviewed articles. She is currently Director of the Cornell Center for Enervating Neuroimmune Disease. Email: mrh5@cornell.edu



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Invest in ME Research

B-cell Research/Rituximab
One Event Can Change Everything



One small charity – one BIG cause
A rituximab clinical trial for ME
www.ukrituximabtrial.org

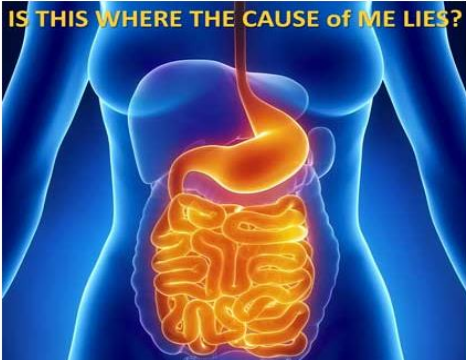
Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. A UK trial of rituximab for ME is being initiated and organised by Invest in ME and University College London.

The charity wishes to establish a Centre of Excellence for ME in the UK. Please support us and help us to help people with ME. **Let's Do It For ME Let's Do Research.**

Invest in ME (UK charity nr. 1114035)
www.investinme.org email: info@investinme.org idifme.org

Small Charity BIG Cause
 Support ME Research Invest in ME

Gut Microbiome
IS THIS WHERE THE CAUSE OF ME LIES?



We'd like to find out!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. This is one project UK Charity Invest in ME wishes to initiate to determine whether changes in the gut microbiota contribute to ME. Other biomedical research projects will follow. Please support our proposal for an examination and research facility for ME in the UK and help us to help people with ME. **Let's Do It For ME.** See - <http://www.investinme.org/research.htm>

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No Isolation



Earlier this year Invest in ME Research were contacted by a Norwegian company who were interested in promoting a product which aimed to reduce the isolation experienced by many younger people who were unable to attend school, or were cut-off from social contact due to illness.

Obviously, the charity immediately saw the parallels with ME and the possibility of raising awareness of one of the least publicised side effects of this disease on patients, and their families.

Our immediate reaction was how we can help

use this to publicise awareness of the effects of ME on children.

We then invited the company – No Isolation – to take a table at the IIMEC12 conference and offered to work further to support this campaign. The charity does not normally advertise products, or businesses, but on this occasion we feel it is a worthwhile cause that could help alleviate some of the unnecessary suffering which careless or ignorant education systems inflict on sick children and their families.



In this article from No Isolation researcher, Oda Opdal Zachrisen, the company's product AV1 is described.

The AV1 robot helps children and youths with ME

In Norway, a small white robot has become a stand-in in the classroom for children and youths suffering from ME. The robot is now available in the UK.

The Norwegian start up No Isolation has developed a robot that helps children and youths with long-term illness

participate in the classroom on their own terms. The robot, called AV1, acts as the students' eyes, ears and voice in the classroom on days where they cannot be physically present.

The student is in control

The student controls the robot with an app on a tablet. When the student raises their hand, a light flashes on AV1's head. The robot can be turned 360 degrees, so the student can see the entire classroom and talk to other students. If the student does not feel like actively participating, they communicate it by turning on a blue light on AV1's head.

AV1 is designed to withstand Childs play, and can join classmates in the playground or on after school visits.

AV1 is already helping ME-patients

Today, more than 170 children and youths are using AV1 in Norway. Children and youths suffering from ME is the largest user group.

Research fellow Jorun Børsting and senior lecturer Alma Leora Culén at the Institute for Informatics, University of Oslo, are researching the technology needs of ME-patients. They have studied the use of AV1 among nine children and youths suffering from

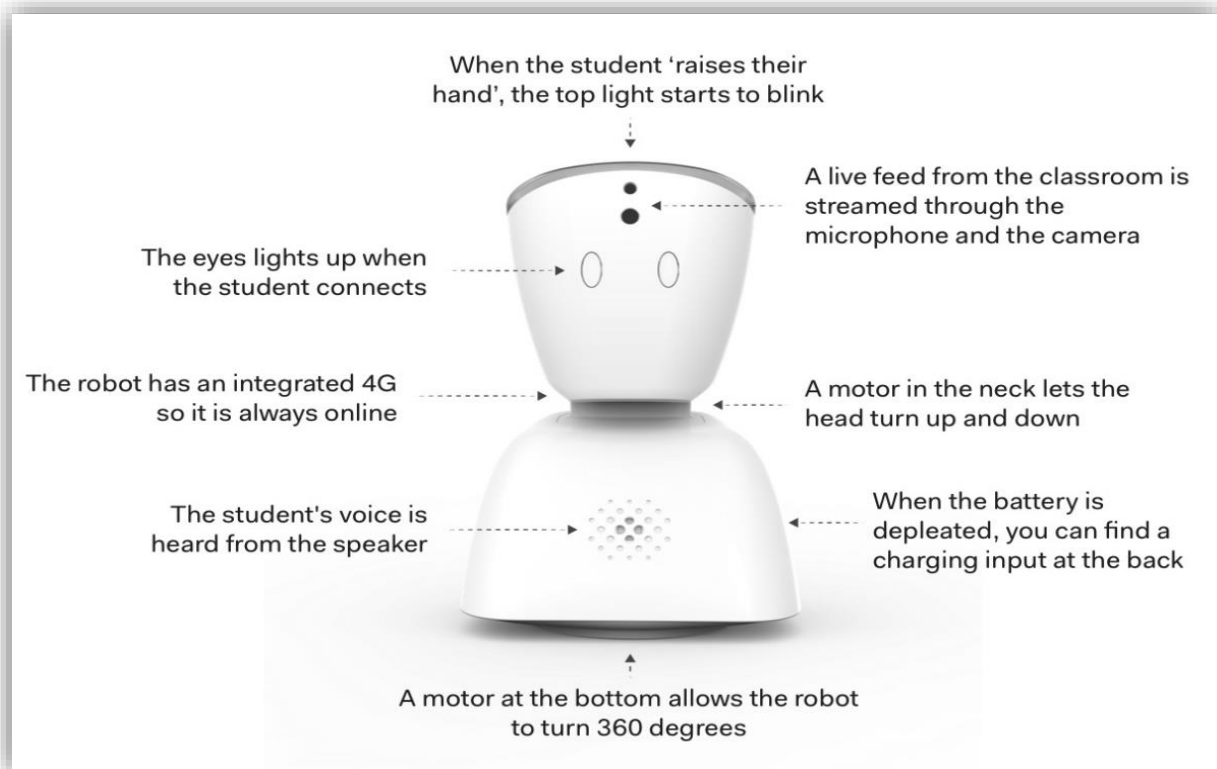
ME.

They see a big advantage in the fact that the robot is designed with ME-patients in mind.

– The advantage in participating in class through a tablet is that they have full control over sound levels, light and movement. In a normal classroom they do not have the option to control sensory inputs in this way. Furthermore, they can participate exactly when they feel like it, taking into account that symptoms can fluctuate over the course of the illness, even from hour to hour, Børsting comments.

Børsting stresses that the robot cannot fully replace normal attendance at school or home teaching, but act as a supplement. – Of the children I followed several had not attended school in a long time when they first received the robot. Some had been out of school for over six months. After they received AV1, all of them participated regularly, on their own terms.

The robot, which has been in use in Norway since autumn 2016, is now available in the rest of Europe. This little helper, which is already underway to children in the UK, can be ordered from No Isolation, at www.noisolation.com





Letter from America

Cuts Threaten Research for Terrible Disease Once Called Chronic Fatigue Syndrome

by **Llewellyn King** Journalist, broadcaster, public speaker

Llewellyn King is the creator, executive producer and host of “White House Chronicle,” a weekly news and public affairs program, airing nationwide on PBS and public, educational and government (PEG) access stations, the commercial AMGTV network, and SiriusXM Radio. King writes a weekly column for the InsideSources Syndicate. King was the founder and publisher of The Energy Daily. The newsletter was the flagship of his award-winning King Publishing Group, which he sold in 2006. The group’s other titles included Defense Week and New Technology Week. In 2011 he created a charity for Myalgic Encephalomyelitis, also known as Chronic Fatigue Syndrome. The charity has a YouTube channel, ME/CFS Alert.

When you are sick, very sick, you wait for medicine to work its magic. But if the disease is Myalgic Encephalomyelitis (ME), you have to wait for the medicine to be invented.

The bad news is that so little funding is going into solving the ME problem, commonly known as Chronic Fatigue Syndrome, that those sick today may be sick for the rest of their lives. They are living a life that is a nearly intolerable to themselves and a massive burden to their loved ones, spouses, parents and caregivers.

What is known is that ME is a disease of the immune system. It is vicious and debilitating, leaving the patient confined to a marginal life, a parallel and unequal existence.

Most infections are of healthy people who are struck down often, but not always, after exercise. The first symptoms can be flu-like: The sufferers feel a few days in bed will do the trick. But having ME is a life sentence. There also have been group infections, known as “clusters,” where hundreds

have been stricken.

If you have ME, the least exertion can force you to spend days in bed, exhausted, hurting in myriad ways from headaches to what one woman described as “feeling like your bones are exploding.”

In severe cases, the patient cannot tolerate light or sound. A young man, newly married, and felled unaccountably, had to live in a closet for an extended period before he could handle light and sound. Symptoms vary but most of the time a victim feels, as one told me, “like you are a car that has run out of gas and your tank cannot be filled up again.” A teenager told me that if she is to go out with friends, she has to weigh that against days of bed rest, in a complete state of collapse.

The National Institutes of Health (NIH) — the principal researcher into ME and dozens of other perplexing diseases — has historically given ME a pittance. In the last three years funding has been held to \$5 million a year, although the Obama



administration had promised more. To put this in perspective, the trade association of the pharmaceutical industry calculates that it costs \$1.2 billion dollars to bring a new drug to market. Sadly that industry has not shown interest in ME, so the research is mostly funded by NIH and private groups and individuals.

The news that the Trump administration is thinking of cutting the total NIH budget by \$5 billion has caused a palpable anxiety to grip the ME community. The disease is cruel enough, does it need to be compounded by the government?

That is why those who could manage it and members of their families were enthusiastic supporters of the March for Science. They were out there with a sense of being at the barricades as the barbarians massed on the other side.

The United States has led the world for years in scientific discovery and implementation. It is deeply disturbing to think that the country would draw back from it. But the administration's

ambivalence is clear. The Department of Energy with 17 national laboratories, every one the envy of the world, is headed by Rick Perry.

When he ran for president, he did so on a plank that included closing the department. The Environmental Protection Agency, with a history of struggling to get the regulatory science right, is headed by Scott Pruitt. As attorney general of Oklahoma, he sought to hobble the agency with lawsuits.

So across science, from the National Aeronautics and Space Administration to the research service of the Department of Agriculture, there is fear among scientists; fear for their jobs, fear for science and fear for America.

In the sick rooms of the 1 million or so ME sufferers, despondency has reached new depths. You will not be cured if no one cares enough to look for a cure.

Can you double down on despair?



Invest in ME Research Visit The CMO of England



Recently Invest in ME Research again invited the Chief Medical Officer of England to our 12th International ME Conference in London [1].

Regrettably, this invitation was declined.

However, after the continued orchestrated and misleading headlines relating to the PACE Trial II on children then we felt a new approach was required.

In England, the CMO is a member of the board of the National Health Service (NHS), a civil servant in the Department of Health, and head of the medical civil service. So this presents us with an opportunity to cover failings in these areas.

We must change the false view of ME constantly being represented by some organisations responsible for funding research and the media. The CMO has a duty to be informed - and support good research and clinical practice.

Invest in ME Research therefore arranged a meeting with the CMO in London which will include our advisors and cover areas such as policy around ME since the last CMO report [3], epidemiology of ME, current/future international research, education regarding ME etc.

Invest in ME Research is already approaching the issues around ME with an international context. We have already engaged with researchers and

clinicians in other countries. Therefore, in this discussion we also used the knowledge and collaborative activities from discussions the charity has had with all of our international contacts.

Along with our colleagues in the European ME Alliance (EMEA) we are looking at ME in Europe and EMEA has been working very hard within the European Federation of Neurological Alliances (EFNA). We are also in continuing discussions with NIH on ways to improve diagnosis, research and treatments for ME. Regarding the CMO meeting - this is a UK problem -and therefore requires a UK strategy. Invest in ME Research therefore also invited the CMOs of Scotland, Northern Ireland and Wales to this meeting.

But a Summit of CMOs for ME - sounded like something that could be useful. All of the UK's CMOs were invited to our 12th International ME Conference 2017 in London

Invest in ME Research had requested a meeting with all four CMOs (England, Wales, Scotland and Northern Ireland) and on Wednesday 11 January 2017 a meeting took place with the Deputy CMO of England Dr Gina Radford at Whitehall Court, London.

Invest in ME Research previously wrote about our intention to engage with the Chief Medical Officers of the UK and appraise them of the research into ME that the charity is facilitating and the current issues which continue to exist and which we believe the CMOs have a duty to confront - [**A Summit of CMOs**](#)

ATTENDEES:

- Dr Gina Radford, Deputy Chief Medical Officer, England
- Professor Jonathan Edwards (UCL)
- Dr Ian Gibson

- Countess Mar
- Fane Mensah (PhD student, UCL)
- Representatives from Invest in ME Research

Apologies:

- Dr Nigel Speight
- CMO Scotland
- CMO Northern Ireland
- CMO Wales

Prior to the meeting the charity had submitted two documents to the CMOs and participants.

One concerning children and the deplorable state that exists as well as case studies of children badly affected by the way that the existing mentality toward ME is allowed to distort proper healthcare. In this document evidence was presented to the CMO of the way many families of children with ME are being harassed and subject to child Protection proceedings.

Though the establishment organisations have totally failed children with ME the harassment is not, however, confined to vulnerable patients or their families either - as witnessed by this story - (<http://investinme.org/IIME-Newslet-1604-NS999.shtml>).

The following document had also been sent prior to the meeting to all attendees - [Summary of developments following CMO's report of 2002](#)

It was agreed that the meeting would take an informal format to allow free discussion and the available agenda would be used as guidance. It was mentioned that Invest in ME Research had sent in information beforehand to allow the CMOs time to familiarise with the issues on the agenda.

Dr Radford said she had read the information given and stated that the CMO could not resolve most of the problems mentioned as the CMO's remit had changed and many of the issues mentioned would be the responsibility of NHS England.

She would, however share the notes with other

CMOs in Wales, Scotland and Northern Ireland.

The charity pointed out that the CMO's remit includes influencing policy and that from experience it seems that ME is not on the CMO's radar.

The charity mentioned that the previous and current CMOs had never accepted the charity's invitations to attend or speak at the international conferences that the charity had organised in the past 11 years.

The invitation was always either too early or too late.

There never seemed to be a right time and this sent a message to patients, carers, researchers and doctors interested in ME that ME was not on the CMO's agenda.

The charity explained that the meeting was taking place and as far as we were concerned, we were talking directly to the CMOs of the UK.

The charity asked directly whether the CMO was happy with the current status of ME research and what was their official opinion on ME?

Dr Radford stated that she could not speak for the CMO and she made the point once again that the CMOs of England, Wales, Scotland and Northern Ireland do not run the NHS. It is the NHS England that runs the services and we would need to discuss these matters with them.

The CMO's relationship with the NHS and remit has changed since 2002 when the 2002 CMO report on CFS/ME was published.

Parameters have changed and now the CMO's remit is to give broadly advice to the government.

The charity read out the publicly stated remit of the CMO such as protect the public, tackle inequality, review policy (mentioned no policy for ME), influence by statements and discussions.

CMO Remit

Countess of Mar said Dr Martin McShane makes nice noises but nothing happens.

The charity described cases provided in the accompanying document where severely ill children with ME who failed to recover with

CBT/GET programmes were then re-diagnosed and given labels such as pervasive refusal syndrome and parents/carers accused of Munchausen Syndrome by Proxy.

The PACE trial was mentioned and Dr Radford had not read PACE.

So Countess of Mar described the well-known shortcomings of the PACE trial including the Information Commissioner's Office being involved leading to a court case to get raw data released and reviewed according to the original protocol and the damage it has caused to the worldwide patient community.

Professor Edwards explained the reasons why the PACE trial and CBT/GET studies were poor science and the system is failing as it allows authors of these papers take on roles as reviewers of the same papers.

The Cochrane review was an example of this.

Dr Gibson described the annual [IIMER Colloquium/Conference](#) and how the science is getting interesting.

There seems to be lack of duty for biomedical research into ME, neglect in taking an all-around approach and ME is not getting its fair share. Dualism was a waste of time and research should open up and the government has failed to take it up.

Fane Mensah described the situation for a young researcher.

He said there needs to be support for young researchers.

Students who are thinking about their career choices need to know there is a future in this exciting and complex field.

He described how the patients he sees as part of the research funded by Invest in ME Research are so grateful that someone is taking them seriously and listens to them.

The charity asked Dr Radford how the CMO made decisions when taking up issues such as antibiotic resistance, Ebola, Zika virus etc.?

Dr Radford said it was because they were major worldwide issues.

The charity said that ME is a major worldwide issue - yet no one knows numbers affected (only rough estimates) and the diagnosis is inaccurate and variable.

Sally Davies should at least make a brief visit to the conference or send a representative to learn about the latest developments.

Dr Clare Gerada as the chair of the Royal College of GPs gave a talk at the [IIMEC8 conference](#) in 2013 and admitted GPs knew very little of ME.

Professor Edwards said ME was a bigger problem than rheumatoid arthritis.

Epidemiology in general was lacking and current service provision was poor.

The direction of ME research has not been founded in good science and the Norwegian phase III rituximab trial results will guide the future.

The psychiatrists do not understand the problem and that is a **BIG** problem.

The PACE trial is a text book case how not to do a trial.

In Practical terms: we need physician led services (very few of which currently exist) which provide help and continued surveillance.

ME is an identifiable problem due to the characteristic of post exertional malaise (PEM). Surveillance is needed as other diseases such as lymphoma can be hidden in that cohort.

Major change has happened in USA, but not in the UK.

Dr Radford asked what we wanted to ask the CMO. The following points were stated -

- Genuinely appreciate the size of the ME problem
- Maintain consultant led services
- Appreciate new research
- Appreciate current services have been hijacked by bogus science and patients find that dispiriting and dangerous

NICE was briefly discussed and a decision whether the guideline will be reviewed should be made by the summer of 2017.

Dr Radford said that it is important there is new

research that they can look at otherwise the guideline remains in a vacuum.

The current recommendation of GET was brought up as harmful and putting children in danger.

The severely ill need information and support. Professor Edwards mentioned MS patients get 6 monthly neurology appointments but ME patients get nothing.

Problems with FITNET were mentioned and Dr Radford was aware of this and stated that FITNET was being reviewed.

Dr Gibson said research is moving toward finding biomarkers.

Metabolomics was proving promising as presented at the [Invest in ME Research international conference](#).

The approach has been too simplistic in the past.

Dr Radford mentioned she is involved in an alliance of rare diseases and that there are hundreds of diseases in the same situation as ME.

The charity said these rare diseases are recognised and patients are not dismissed and stigmatised by the establishment the way ME patients are. ME patients' healthcare complaints, unrelated to ME, are often ignored and dismissed due to the patient's ME label.

The importance of accurate diagnosis with careful history taking was mentioned as endocrine disorders are often misdiagnosed as ME.

Actions

Dr Radford finished the meeting by summing up action points

Highlight emerging research (relevant for NICE guidelines)

Mention liMER colloquium/conference to people of influence

Agree that a new meeting arranged by the charity will take place later in the year when the Norwegian rituximab trial results would be known by the team involved.

liMER Summary

Did we expect more from the visit with the CMO?

Of course!

Our aim is not to have just a cosy chat and keep the status quo. Action is required.

As we stated before ME is a UK/worldwide problem - we did expect (and request) that all UK CMOs attend.

But we have the CMO's attention now, to some extent. We will not leave it alone.

We have a follow-up meeting planned and we will ensure that the CMOs of UK do not remain in the dark about the seriousness or severity of the issues with this disease.

PostScript:

At the CMO's suggestion the charity contacted Simon Stevens of NHS England and Sir Bruce Keogh. At the current point in time we have to state that the treatment of our request for a meeting by Sir Bruce has been not just disappointing but appallingly apathetic to the plight of people with ME and their families.

References

- ▶ [Articles on PACE Trial](#)
- ▶ [Articles on ME/CFS by Margaret Williams and Professor Malcolm Hooper](#)

Summary of developments following CMO's report of 2002

The ME community were by and large delighted at the contents of this Chief Medical Officer's Report in 2002, with its strong implicit acceptance of ME/CFS as a primarily organic/biological illness. The members of the psychiatric viewpoint were sufficiently disheartened by this to refuse to sign up to the report's conclusions.

In 2004 the RCPCH (Royal College of Paediatrics and Child Health) published paediatric guidelines which were very much in line with the CMO's report.

In 2007 NICE guidelines came out, and for all the criticism of these guidelines, regarding their overemphasis of suggested merits of CBT and GET, these also cemented the concept of ME/CFS as an organic illness and made it "official".

What went wrong post 2002?

First and foremost, there was an abdication on the part of adult medicine of responsibility for this condition. This must have been partly due to the tendency to specialisation on the part of even DGH physicians.

No specialty would accept responsibility. In particular, the neurologists were very reluctant to be involved despite the WHO's having designated ME as a neurological disease.

The main problem was that there was no "ology" for ME, neither was one created.

This failure on the part of general medicine had a knock on effect on general practice. GP's sensed the reluctance of physicians to accept referrals, thus making ME less of an official disease and more of a "controversial" condition.

These factors mitigated against the positive recommendations of the above three reports/guidelines.

Secondly, and as a result of this abdication by adult medicine, when specialist ME centres were set up very few medical specialists came forward, and the only people eager to step into the vacuum were the psychiatrists. (Two exceptions to this rule were in Newcastle and Epsom and St Helier, where immunologists took the lead).

There has been widespread patient dissatisfaction with most of these centres. Firstly, the patients seldom saw an actual doctor to at least receive an official medical diagnosis. Secondly, the only support on offer consisted of different forms of CBT and GET which patients found either ineffective or harmful depending on the variety of therapy offered.

The very existence of these specialist centres, of course, removed the obligation of DGH physicians and paediatricians to actually see, diagnose, help and support ME patients.

Thirdly and most importantly, the psychiatric lobby made a concerted counterattack to recover their lost ground. This was all the more effective for being indirect.

Their strategy consisted of the following

1) Ensuring that they were well positioned to influence medical education, both undergraduate and postgraduate.

Again, they were filling a vacuum left by organic medicine.

The two major medical textbooks (The Oxford textbook of Medicine and Kumar and Clark) have chapters on ME/CFS written by psychiatrists and buried in the section on "Functional illness" or "Medically unexplained symptoms")

Of course, the term "ME" is gradually airbrushed out of the narrative and does not occur in the indexes.

Likewise, the major paediatric text Forfar and Arneil had a section on CFS placed in the section

on Child Psychiatry where it is stated baldly “CFS is the commonest psychosomatic illness in adolescence”

2) Use of the term “Biopsychosocial approach” as a further means of muddying the waters. (No one can object to the concept of a “biopsychosocial approach” in theory, as it is just another word for an holistic approach to any patient. However, the psychiatric lobby tend to use it excessively in their approach to ME/CFS, and then seem to forget the “bio” component!

3) Monopolising research and funding for ME/CFS for their own psychiatric agenda. Enormous sums have been involved and large research empires have been created. This all centres round CBT and GET, which have recently been called into question with major criticisms of the PACE trial.

Again this has all happened because of the dearth of alternative proposals from those wishing to do research aimed at biological factors.

(we should note that this, in turn, has been caused by the total lack of funding given to those biomedical research proposals which have been made – thus influencing attitudes in academia)

4) As already mentioned, the specialist centres are largely run by psychiatrists and psychologists.

All this activity is carried on as if the CMO’s

report and NICE Guidelines did not exist, and as if there was not a growing body of evidence for biological causation of ME/CFS. Regarding the patient community, the psychiatric group steadfastly avert their gaze from the large number of severely affected patients, none of whom have responded to CBT or GET

The current state of affairs -

- One still hears GPs saying “we don’t believe in ME in this practice”
- Adult patients have difficulty obtaining an official diagnosis of ME/CFS, and this can lead to them being deprived of benefits
- ME/CFS has effectively been downgraded from being an official medical condition to one that is unofficial and “controversial”
- There are a large number of severely affected adult patients and young people who are being neglected by the profession. Both GPs and consultants frequently refuse to do home visits on patients who are too unwell to attend surgery/outpatients.
- Most distressingly, a significant number of families of children with ME/CFS are being subjected to “Abuse by professionals” (see attached paper)
- Virtually no doctors are coming forward to establish an “ology” for ME

Final anecdote

A GP phones an ME helpline for advice. He says “ I’m really worried I have developed ME”.

Adviser clucks sympathetically.

GP “That’s not the main problem – it’s just that I don’t know what to say to my colleagues” Further sympathetic cluck.. “You see, it has always been a policy of our practice to treat patients with ME with unremitting hostility, ridicule and rejection....So I can’t face telling my colleagues. I think I will just tell them I am suffering with depression”!



www.investinme.org

THE PACE TRIAL

THE PACE Trial has been frequently discussed in articles on the Invest in ME Research website and on the charity's social media since the first paper was published by Lancet in 2011. [1]

The PACE Trial has been shown to be flawed and a colossal waste of scarce public funding which should have gone to funding biomedical research which, by now, may well have been leading to a breakthrough in treating this disease.

Recently the results from this trial have been thoroughly analysed and destroyed by a series of articles published in Professor Vincent Racaniello's (Columbia University, USA) Virology blog by US journalist David Tuller. [2]

Once these reviews began to create huge interest over the internet then the usual typical orchestrated media reaction appeared. As always happens the establishment media trot out their normal array of buffoons and denialists – spreading more oil on the fire by linking ME patients with militants and those who see stigma in mental health – with no real evidence to support either accusation and demonstrating a profound ignorance of the disease and of ME patients [3].

But then the establishment view is to see any valid criticism against false science as a threat - and their only method of response is to denigrate those who are suffering the most.

Despite an orchestrated attempt to maintain the pretence that anything valid was produced by this research it must surely be plain for all to see, including a great many more academics and unbiased opinion, that the PACE Trial is now synonymous with farce, bias and null field research.

On October 27th the Information Commissioner's Office (ICO) ruled in favour of a complainant that had requested raw data from the PACE trial to be made publicly available by the QMUL. [4]. In attempting to thwart attempts via FOI to get PACE Trial data released QMUL spent, in one month, over twice as much money as patients raised in three years of fundraising for liMER's biomedical research foundation project.

As our advisor Emeritus Professor Jonathan Edwards from UCL has written -

"If scientific interpretation is poor it deserves no protection. If it is good it needs none."

The MRC policy is unequivocal on this – as pointed out by James Coyne PhD [Why the scientific community needs the PACE trial data to be released Posted November 11, 2015] [5]

The UK Medical Research Council (MRC) 2011 policy on data sharing and preservation has endorsed principles laid out by the Research Councils UK including

"Publicly funded research data are a public good, produced in the public interest, which should be made openly available with as few restrictions as possible in a timely and responsible manner.

To enable research data to be discoverable and effectively re-used by others, sufficient metadata should be recorded and made openly available to enable other researchers to understand the research and re-use potential of the data. Published results should always include information on how to access the supporting data."

-UK Medical Research Council (MRC) 2011 policy on



data sharing and preservation

So it is even more incongruous that, in all of the recent discussions, the MRC and other funders of this trial were so silent regarding this clear breach of guidance, this utter waste of money, this total waste of years of opportunity for good research into ME?

Although it does not surprise us the silence is, nevertheless, indicative of an establishment organisation whose policy toward ME research is being led by those who do not best serve the interests of patients.

Retraction of the PACE trial paper and release of the raw data for other scientists to review would no doubt mean that the whole mess around the PACE trial would have consequence elsewhere - as it is not just about one paper but the influence that it has had on health policies across the world.

It would, however, send a strong message that misleading research is not tolerated nor should it be used as a means to bolster a universities' Research Excellence Framework (REF) as has been the case now.

The seriousness of the way in which this whole research has been conducted, and the consequences still remaining as referenced research, requires that the PACE Trial paper itself has to be retracted.

Retracting the whole paper will send a message that poor quality research, especially when it is designed to influence healthcare policy, cannot be allowed.

The Lancet, which fast-tracked the first of the PACE trial papers in 2011, really ought to have favoured patients. The editor of the Lancet failed even to respond to Invest in ME Research's letters regarding the PACE trial

<http://www.investinme.org/Documents/Lancet/Letter%20to%20Editor%20of%20the%20Lancet%20November%202015.pdf>

[ber%202015.pdf](http://www.investinme.org/Documents/Lancet/Letter%20to%20Editor%20of%20the%20Lancet%20November%202015.pdf)

In this day and age it is unacceptable that research performed with public funding can be allowed to be controlled by anyone who is not transparent and open in their treatment of data related to the research.

If raw data from the trial shows that the public has been misled even more than so far identified then there should be a public inquiry

The MRC invests in research on behalf of the UK tax payer. The taxpayer has been ill-served by the PACE Trial. The MRC should therefore examine the possibility of having the funds for the PACE Trial returned in part or in full to the public – and from there to be allocated to biomedical research into ME.

It must be considered whether the Principal Investigators of the PACE Trial be barred from receiving any further public funding for future research into ME.

The MRC need to review the management of this trial and procedures for deciding how funding for research into ME is decided to be allocated.

The refereeing system for reviewing research applications for ME needs to be overhauled and made transparent.

Those in the MRC who have been responsible for research into ME over the last eleven years must, if still in positions of influence with regard to ME research, be replaced. The MRC policies have been a shambles and valuable years of research possibilities have been wasted - along with a monumental loss of scarce public funding.

Conflicts of interest of those in the MRC who have any influence on ME research need to be declared and examined.

Consideration ought to be made for a government inquiry, or parliamentary committee to scrutinise the conduct of the MRC with regards to its policies, research grant applications and grants for ME made over the last 13 years since the CMO's report was made.

We are sure none of this will happen. The establishment looks after its own.

But it seems impossible to see how, after the way the MRC has operated over the last ten years, ME patients or carers or ME patient groups or ME charities could possibly have any faith in an organisation such as this unless it is reformed. We fail to see how any healthcare professional or researcher can have faith in the Lancet until the PACE Trial is recognised for the farce that it has become.

Professor Jonathan Edwards wrote the following

“The PACE trial of cognitive behavioural therapy and graded exercise therapy for chronic fatigue syndrome/myalgic encephalomyelitis has raised serious questions about research methodology. An editorial article by Geraghty gives a fair account of the problems involved, if anything understating the case. The response by White et al. fails to address the key design flaw, of an unblinded study with subjective outcome measures, apparently demonstrating a lack of understanding of basic trial design requirements. The failure of the academic community to recognise the weakness of trials of this type suggests that a major overhaul of quality control is needed.”

<http://journals.sagepub.com/doi/full/10.1177/1359105317700886>

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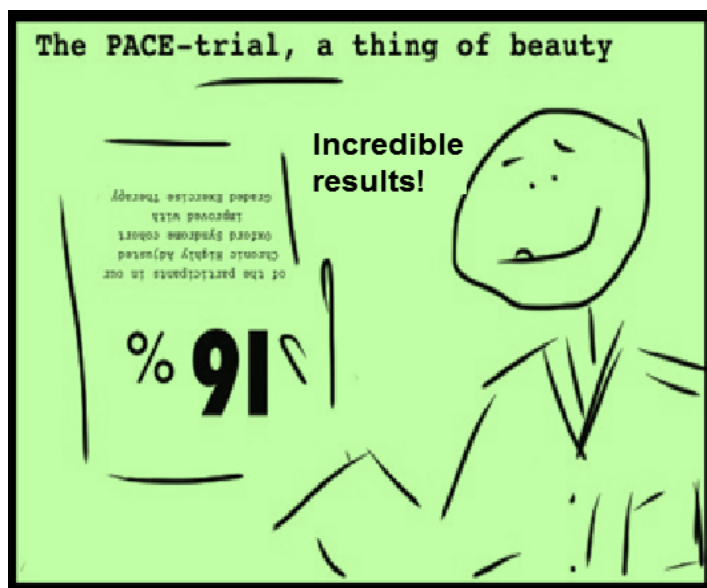
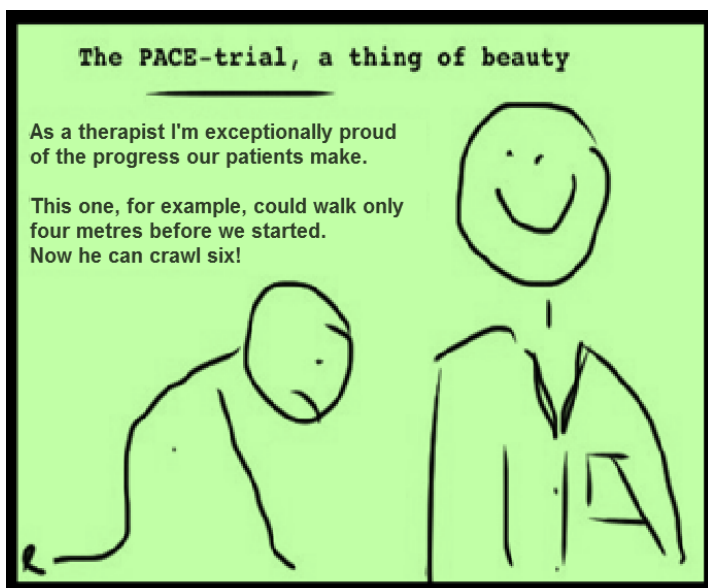
An open letter to Psychological Medicine about “recovery” and the PACE trial

A letter, for which Invest in ME Research helped in obtaining signatures from some of the top scientists, was recently published and sent to Psychological Medicine . The letter included signatures from eminent scientists and researchers from institutions including the following -

- | | | |
|--|---|--|
| HHV-6 Foundation | National Cancer Institute USA | Georgetown University |
| University of California | Bateman Horne Center | University of British Columbia |
| DePaul University | EVMed Research | Stanford University |
| University of Medicine and Dentistry of New Jersey | | Tulane University School of Medicine |
| University of Manchester | George Mason University | University of East London |
| Cornell University | University of Sunderland | Harvard Medical School |
| Ithaca College New York | Nova Southeastern University | Hunter-Hopkins Center |
| University of Kent | Columbia University | Duke University School of Medicine |
| Stichting Cardiozorg | University of Utah | Nevada Center for Biomedical Research |
| Northwestern University | Pritzker School of Law | University of Oslo |
| University of Minnesota | National Centre for Neuroimmunology and Emerging Diseases | |
| George Mason University | Solve ME/CFS Initiative | Stanford University School of Medicine |
| Tufts University | Linköping University | Rutgers New Jersey Medical School |
| WorkWell Foundation | Catholic University of Valencia School of Medicine | |
| University of Calgary | Rutgers Robert Wood Johnson Medical School | |
| University of Cumbria | Soerabaja Research Center | University of Birmingham |
| London School of Hygiene & Tropical Medicine | | Victoria University of Wellington |

Also signing were organisations from around the world such as Invest in ME Research and our partners in the European ME Alliance, Open Medicine Institute. Also from UK individuals such as - Simon Duffy (Director Centre for Welfare Reform), Jonathan C.W. Edwards, MD (Emeritus Professor of Medicine University College London) and Ian Gibson, PhD (Former Member of Parliament for Norwich North Former Dean, School of Biological Sciences University of East Anglia).

The letter (shown on the following page) demonstrates the gathering weight of scientific opinion exposing the PACE Trial.



from “MEDICINE and ME” <http://www.investinme.org/IIME-Cartoons-2013-01.shtml>

13 MARCH 2017

Sir Robin Murray and Dr. Kenneth Kendler

Psychological Medicine

Cambridge University Press

University Printing House

Shaftesbury Road

Cambridge CB2 8BS

UK

Dear Sir Robin Murray and Dr. Kendler:

In 2013, *Psychological Medicine* published [an article](#) called “Recovery from chronic fatigue syndrome after treatments given in the PACE trial.” [1] In the paper, White et al. reported that graded exercise therapy (GET) and cognitive behavioural therapy (CBT) each led to recovery in 22% of patients, compared with only 7% in a comparison group. The two treatments, they concluded, offered patients “the best chance of recovery.”

PACE was the largest clinical trial ever conducted for chronic fatigue syndrome (also known as myalgic encephalomyelitis, or ME/CFS), with [the first results](#) published in *The Lancet* in 2011. [2] It was an open-label study with subjective primary outcomes, a design that requires strict vigilance to prevent the possibility of bias. Yet PACE suffered from [major flaws that have raised serious concerns](#) about the validity, reliability and integrity of the findings. [3] Despite these flaws, White et al.’s claims of recovery in *Psychological Medicine* have greatly impacted treatment, research, and public attitudes towards ME/CFS.

According to [the protocol for the PACE trial](#), participants needed to meet specific benchmarks on four different measures in order to be defined as having achieved “recovery.” [4] But in *Psychological Medicine*, White et al. significantly relaxed each of the four required outcomes, making “recovery” far easier to achieve. No PACE oversight committees appear to have approved the redefinition of recovery; at least, no such approvals were mentioned. White et al. did not publish the results they would have gotten using the original protocol approach, nor did they include sensitivity analyses, the standard statistical method for assessing the impact of such changes.

Patients, advocates and some scientists quickly pointed out these and other problems. In October of 2015, *Virology Blog* published [an investigation of PACE](#), by David Tuller of the University of California, Berkeley, that confirmed the trial’s methodological lapses. [5] Since then, more than 12,000 patients and supporters have signed a petition calling for *Psychological Medicine* to retract the questionable recovery claims. Yet the journal has taken no steps to address the issues.

Last summer, Queen Mary University of London released anonymized PACE trial data under a tribunal order arising from a patient’s freedom-of-information request. In December, an

independent research group used that newly released data [to calculate the recovery results](#) per the original methodology outlined in the protocol.[6] This reanalysis documented what was already clear: that the claims of recovery could not be taken at face value.

In the reanalysis, which appeared in the journal *Fatigue: Biomedicine, Health & Behavior*, Wilshire et al. reported that the PACE protocol's definition of "recovery" yielded recovery rates of 7 % or less for all arms of the trial. Moreover, in contrast to the findings reported in *Psychological Medicine*, the PACE interventions offered no statistically significant benefits. In conclusion, noted Wilshire et al., "the claim that patients can recover as a result of CBT and GET is not justified by the data, and is highly misleading to clinicians and patients considering these treatments."

In short, the PACE trial had null results for recovery, according to the protocol definition selected by the authors themselves. Besides the inflated recovery results reported in *Psychological Medicine*, the study suffered from a host of other problems, including the following:

*In a paradox, the revised recovery thresholds for physical function and fatigue—two of the four recovery measures—were so lax that patients could *deteriorate* during the trial and yet be counted as "recovered" on these outcomes. In fact, 13 % of participants met one or both of these recovery thresholds at baseline. White et al. did not disclose these salient facts in *Psychological Medicine*. We know of no other studies in the clinical trial literature in which recovery thresholds for an indicator actually represented worse health status than the entry thresholds for serious disability on the same indicator.

*During the trial, the authors published [a newsletter for participants](#) that included glowing testimonials from earlier participants about their positive outcomes in the trial.[7] An article in the same newsletter reported that a national clinical guidelines committee had already recommended CBT and GET as effective; the newsletter article did not mention adaptive pacing therapy, an intervention developed specifically for the PACE trial. The participant testimonials and the newsletter article could have biased the responses of an unknown number of the two hundred or more people still undergoing assessments—about a third of the total sample.

*The PACE protocol included a promise that the investigators would inform prospective participants of "any possible conflicts of interest." Key PACE investigators have had longstanding relationships with major insurance companies, advising them on how to handle disability claims related to ME/CFS. However, the trial's consent forms did not mention these self-evident conflicts of interest. It is irrelevant that insurance companies were not directly involved in the trial and insufficient that the investigators disclosed these links in their published research. Given this serious omission, the consent obtained from the 641 trial participants is of questionable legitimacy.

Such flaws are unacceptable in published research; they cannot be defended or explained away. The PACE investigators have repeatedly tried to address these concerns. Yet

their efforts to date—in journal correspondence, news articles, blog posts, and most recently in [their response](#) to Wilshire et al. in *Fatigue*[8]—have been incomplete and unconvincing.

The PACE trial compounded these errors by using a case definition for the illness that required only one symptom—six months of disabling, unexplained fatigue. A [2015 report](#) from the U.S. National Institutes of Health recommended abandoning this single-symptom approach for identifying patients.[9] The NIH report concluded that this broad case definition generated heterogeneous samples of people with a variety of fatiguing illnesses, and that using it to study ME/CFS could “impair progress and cause harm.”

PACE included sub-group analyses of two alternate and more specific case definitions, but these case definitions were modified in ways that could have impacted the results. Moreover, an unknown number of prospective participants might have met these alternate criteria but been excluded from the study by the initial screening.

To protect patients from ineffective and possibly harmful treatments, White et al.’s recovery claims cannot stand in the literature. Therefore, we are asking *Psychological Medicine* to retract the paper immediately. Patients and clinicians deserve and expect accurate and unbiased information on which to base their treatment decisions. We urge you to take action without further delay.

Sincerely,

[1] White PD, Goldsmith K, Johnson AL, et al. 2013. Recovery from chronic fatigue syndrome after treatments given in the PACE trial. *Psychological Medicine* 43(10): 2227-2235.

[2] White PD, Goldsmith KA, Johnson AL, et al. 2011. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *The Lancet* 377: 823–836

[3] Racaniello V. 2016. An open letter to The Lancet, again. *Virology Blog*, 10 Feb. Available at: <http://www.virology.ws/2016/02/10/open-letter-lancet-again/> (accessed on 2/24/17).

[4] White PD, Sharpe MC, Chalder T, et al. 2007. Protocol for the PACE trial: a randomised controlled trial of adaptive pacing, cognitive behaviour therapy, and graded exercise, as supplements to standardised specialist medical care versus standardised specialist medical care alone for patients with the chronic fatigue syndrome/myalgic encephalomyelitis or encephalopathy. *BMC Neurology* 7: 6.

[5] Tuller D. 2015. Trial by error: the troubling case of the PACE chronic fatigue syndrome trial. *Virology Blog*, 21-23 Oct. Available at: <http://www.virology.ws/2015/10/21/trial-by-error-i/> (accessed on 2/24/17)

[6] Wilshire C, Kindlon T, Matthees A, McGrath S. 2016. Can patients with chronic fatigue syndrome really recover after graded exercise or cognitive behavioural therapy? A critical

commentary and preliminary re-analysis of the PACE trial. *Fatigue: Biomedicine, Health & Behavior*; published online 14 Dec. Available

at: <http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1259724> (accessed on 2/24/17)

[7] PACE Participants Newsletter. December 2008. Issue 3. Available

at: <http://www.wolfson.qmul.ac.uk/images/pdfs/participantsnewsletter3.pdf> (accessed on 2/24/17).

[8] Sharpe M, Chalder T, Johnson AL, et al. 2017. Do more people recover from chronic fatigue syndrome with cognitive behaviour therapy or graded exercise therapy than with other treatments? *Fatigue: Biomedicine, Health & Behavior*; published online 15 Feb. Available at: <http://www.tandfonline.com/doi/full/10.1080/21641846.2017.1288629> (accessed on 2/24/17).

[9] Green CR, Cowan P, Elk R. 2015. National Institutes of Health Pathways to Prevention Workshop: Advancing the research on myalgic encephalomyelitis/chronic fatigue syndrome. *Annals of Internal Medicine* 162: 860-865.

IiMER Conference DVDs

The Invest in ME Research conference DVDs are professionally filmed and authored DVD sets consisting of four discs in Dolby stereo.

They contain all of the presentations from Invest in ME Research International ME/CFS Conferences (2006 – 2015). Also included in the DVD sets are interviews with ME presenters, news stories, round-table discussions or pre-conference dinner presentations.

The Invest in ME Research conference DVDs have been sold in over 20 countries and are available as an educational tool – useful for healthcare staff, researchers, scientists, educational specialists, media, ME support groups and people with ME and their carers/parents. Full details can be found at -

<http://www.investinme.eu/IIMEC11.shtml#dvd>

or via emailing Invest in ME Research at

<mailto:info@investinme.org>



MARGARET WILLIAMS REPOSITORY

www.margaretwilliams.me

What we are witnessing now is the gradual destruction of the flawed and negligent perception of ME, which vested interests have created for the last decades in UK and elsewhere and which has so pervasively influenced government departments, academia, medical establishments, the media and, by eventual lemming-like acceptance, the public. The flagship of the those who have promoted (and benefited) from the biopsychosocial view of ME for so long has begun to sink, run aground on the rocks of reason, science and an intractable dedication from some patient organisations and patient advocates.

The wreck that is PACE is now dragging down those pillars of the establishment that have supported it. For so many years when establishment organisations and individuals have been following a false path of research and treatments for ME, supported by fickle media editors and buffoon, journalist hacks, there was a constant source of information and analysis about ME - a voice of science, reason, and factual evidence that gave the lie to the biopsychosocialists.

This came from **Margaret Williams** - a severely affected, but articulate patient who saw through the falsehood of the myths perpetrated by vested interests and produced countless articles exposing the corrupt environment maintained by the establishment toward ME.

Invest in ME Research has featured many of Margaret Williams' articles during its 11 years as a charity.

Now all of her articles have been indexed and made available online at this URL

www.margaretwilliams.me

Not only is this compendium of articles and information fully indexed but the website also contains a search button enabling one to search on any topic, organisation or individual very easily.

This is a resource that will be of historical significance for academics - and a huge testament to one of the great ME advocates.

You don't have to be go crazy to raise funds for Invest in ME Research – simple things such as a North Pole marathon, Everest Base Camp, 28 EU marathons Look at current and past fundraising events

<http://www.investinme.org/fundraising.shtml>

<http://www.investinme.org/prev-fundraising.shtml>



BREAKFAST in BRUSSELS

www.euro-me.org

EUROPEAN ME ALLIANCE NEWS

Summary Report Breakfast Colloquium

European Parliament –

Brussels March 7th 2017

The European ME Alliance recently organised a meeting in the European Parliament to discuss the situation with regard to ME in Europe.

This event followed meetings for clinicians on the day before organised by EMEA-Belgium member [ME Association].

The intent with the meeting – labelled **Breakfast in Brussels** – was to make European MEPs aware of the lack of services for people with ME, the negligible amount of proper research being carried out into the disease across Europe, and the lack of funding given to biomedical research into the disease and the waste which is being given to flawed psychiatric theories which have caused harm to patients across the continent.

With the help of MEP, Mrs. Helga Stevens and her staff the Belgian ME Association coordinated the event that consisted of a number of selected speakers addressing a gathering of MEPs.

The speakers were Dr. Ian Gibson, Dr. Olli Polo, Dr. Nigel Speight, Dr. Louise Brinth and CRPD Expert Dr. László Lovász – who shared their knowledge and expertise with the audience.

The following are extemporaneous notes compiled by EMEA Belgium during the meeting.



BREAKFAST in BRUSSELS

www.euro-me.org

Welcome by host

MEP Mrs. Helga Stevens



MEP Mrs. Helga Stevens thanked everyone for attending, and thanked EMEA for letting her host this event and for organising this important Breakfast Colloquium at the European Parliament.

She started by saying that Myalgic Encephalomyelitis (ME) is a very serious, disabling and chronic organic disorder classified by the World Health Organisation as a distinct neurological disorder since 1969 and that ME is often denigrated and denied by doctors, policy-makers and the general public.

This is why the classification as a neurological disease is an important step towards broader official recognition by the medical and scientific establishment!

Personally, she found it very interesting not to look at the disease from a medical point of view but also in terms of it potentially being recognised and understood as a disability and from a social model of disability point of view whereby it is the environment that is disabling rather than victimising the individual him/herself.

Mrs. Stevens looked forward to learning more about ME, in particular about children with ME and what good practice examples exist out there. She wished EMEA all the best for the event.



Dr. Ian Gibson – European Issues

Dr. Ian Gibson talked about public disability problems and how those are supported, not just in the Member States but across the European Parliament as well.



He referred to Professor Tom Shakespeare (at University of East Anglia) who shows that much of the determination of policy on illness depends on trying to stop people with illnesses getting benefits. Rather than judging whether a person has a practical chance of being able to find a job the new capability assessment investigates whether the person has the ability, in theory, to do any form of work at all. Most likely the eligibility criteria can substantially make it more difficult for people to access benefits.

Politicians have a predisposition to try and save money and in this area definitions are extremely important in determining whether patients get benefits or not. Putting money into biomedical research, Dr. Gibson said, is much more expensive - even though it might be more productive in the long run and save a lot of money. In the short term, it is about trying to get definitions.

Going over to therapy Dr. Gibson touched upon a paper called "The PACE Trial" which is been looked at now by some very serious academics in the United Kingdom and has been discredited. When asking questions in the House of Commons they did not receive any credible answers. On the other hand there was huge support for the MP who asked these very pertinent questions about these decisions, why they were made and about disability and benefits. He became a hero in the ME community.

The economic consequences of not being

diagnosed at an early stage are increasing by the minute, but the research may bring about something in that field. We are not there yet, but we need to support the research that is going on. The Americans have calculated that across the world hundreds of billions of pounds/euro's in benefits are not being given to people who are not being able to work.

Dr Ian Gibson said there are two things for which the UN in developing countries could be supportive. Firstly, the WHO should be able to organise activities to support ME and its patients. Because there is money there and they have worked on diagnosis, treatment and care before e.g. in polio. Secondly, they have defined ME as a neurological problem but nothing is being done about it. So some of us are working very hard to change that. He also mentioned the WHO ICD-classification is still being looked at.

The main issue for politicians to consider is the millions of people that have been classified with ME and remember that their lives are being ruined together with that of their families.

However, to the question of how many people we are talking about, there is no answer because of lack of any registered data. So we do not really know how many patients have ME but the estimate is about 25 million patients around the world.

ME is not recognised or being taken seriously. However, scientific research is finally going ahead and showing progress. It is mostly funded by private money, charities and other organisations and we have to find ways to increase this. The Americans are joining in, and are coming to the Invest in ME Research conference in London, which takes place for the 12th year now in June. At the conference patients and scientist are there together and it is amazing to see them talking to each other because doctors do not like talking to patients because of the difficult questions that are asked. It is also great to show people there is progress. The Norwegians are on the way to making a change for the patients.

Conclusion

Many people out there need your support, and benefit from the exchange of different countries and that is something too to bear in mind when one thinks about ME. It is not just the illness itself but also the effect it has on millions of peoples' lives and the realisation that nothing has changed over the last ten years. Nevertheless, it is starting to change now.



Dr. Olli Polo – MD's View of ME

How patients with ME are seen by doctors without any particular knowledge of the disease?



Myalgic Encephalomyelitis is a very particular condition and the normal concepts

that one can apply to many other diseases cannot be applied here. This is clearly due to the misunderstanding about this disease. Last week one of his patients said: "Going to the doctor, is like going to the court. The doctor is the judge and the patient is guilty." Dr. Olli Polo wondered if this was true, but there are stories that corroborate this based on the way doctors with a lack of knowledge of ME treat patients.

The behaviour of doctors towards ME patients is characterised by loss of contact with reality, altered values and social interaction impairment. Doctors say that their patients are somaticizing their mental symptoms but now we actually know that the doctor is psychiatrizing the patient's traumatic symptoms. Normally, doctors run the research but, in this case, the patients ask for research and recognition for ME as a real disease. Patients are

then confronted with the resistance of the medical society to get into this.

Investment in medical research is decreasing overall and we are also producing more doctors with differing standard levels of knowledge because they no longer have a scientific background. We have a few written treatment guidelines that should set the minimum level of standard care in primary care and regional hospitals. If patients cannot be treated according to the guidelines then they are referred to the university hospitals. However, the reality today is that, after twenty years, public health care is only provided and available treatment at the university hospitals.

In other words, one can only receive evidence based diagnostics and treatments, so if a treatment works but is not in the guidelines one is not entitled to receive this treatment. This makes doctors afraid of regulatory actions (e.g. we had an eleven year old, paralysed girl, who had to be taken to Holland – Rotterdam to get Immunoglobulin-IV treatment.). There is actually written evidence about the use of this therapy in ME but in Finland no one dares to give it or fear of regulatory actions.

Doctors who are interested in studying or treating ME/CFS experience the same faith as patients. The doctors lose their credibility, their jobs and jeopardised by the medical establishment. The Finnish health professionals state that the purpose of a health professional is to maintain health, prolong health, heal sick patients and alleviate their suffering. Also in his professional activity he must apply commonly accepted, experience-based, medically acceptable procedures, before giving any medication to a patient which must be continuously updated.

Therefore, a research-orientated doctor/scientist may arrive in a contradictory situation, where commonly accepted procedures are more about about promoting health than alleviating suffering of the patient. So what to do? For instance, if an ME patient is misdiagnosed with depression then, unfortunately, they have little expectation other than the increase of exercise, despite the

worsening of symptoms, just in order to get social benefits. Patients who are malnourished are proposed Graded Exercise Therapy to improve their fitness.

If a doctor fails to alleviate suffering, or fails to use experience-based accepted procedures and medication then the doctor will be subject to regulatory actions. This is also applied by the Ethical Review Board (ERB). Evidence-based medicine has gone somehow too far. There is no evidence-based treatments when treatments are being used for the first time. So they are experimental treatments, and the possibility to carry out these treatments calls for innovations as they are advancing science very much.

Nowadays we speak a lot about personal medicine versus quality medicine.

In USA some doctors have been sued for their innovative and experimental treatments. This could happen in Europe.

A physician and surgeon should not be subject to disciplinary action solely on the basis that the advice or the treatment he/she rendered to the patient is an alternative or complementary medicine, as long as that treatment or advice meets all the following requirements:

- There is informed consent
- The patient knows he/she is not getting evidence-based standard medical care
- they have been fully informed of what the conventional treatments available are
- they have been informed of any side effects that may still be allowed but not cause delay in traditional treatments or cause death or bodily injury

Conclusion

The medical community is getting more and more regulated which is understandable if the educational level of doctors is decreasing. However, at the same time, we should be careful not to throw out the baby with the bathwater for those who are innovative and practise medicine

with true ethical principles, which they have learned in medical school, in order to help the patients using all their means. If we are intelligent and innovative, why do we not use our qualities just to try to help the patient?



Dr. Nigel Speight Children with ME

Dr. Nigel Speight thanked the Parliamentarians for the opportunity to speak at the European Parliament. A lot has already been said on the basic issue about ME being an organic disease and for him one of the beauties of working with children is they highlight this fact.



Dr. Speight once told an adult neurologist that he had an interest in paediatric ME. The neurologist replied: "Oh, I didn't realise that it occurred in children, maybe I should think again."

In other words the neurologist had the common view that all adults with ME were just depressive losers but if children can get ME, that would make him think again. Dr. Speight says his experience with working with children and seeing happy, healthy, cheerful, sociable children struck down with ME for him is the biggest proof one can have of ME being fundamentally an organic process.

He actually accumulated over 600 cases of ME over the last 30 years mainly within the United Kingdom but has also been to Ireland, Norway and Germany.

Dr. Nigel Speight briefly shared some of his clinical experience but what he really wanted to talk about

was the abuse that families of children with ME suffer as a result of doctors not protecting them properly. Over 30 years he had been involved with 40 families who had been subject to child protection proceedings reaching case conference level, sometimes court proceedings, to remove children. Fortunately, he has been successful in 38 cases but lost one in England and one in Norway. Each case was a tragedy.

Dr. Speight showed some slides of a follow up study showing progress over time of 49 patients, of which 15 recovered over two to five years. Seven of them who were unlucky and were getting worse, and a large number who were going up and down. ME is a very unpredictable condition, with wide fluctuations in severity. Overall, there is grounds for cautious optimism and the prognosis is probably slightly better in children than in adults.

Apart from what we can learn from the fact that children can get ME, he thinks the severe cases of ME teach us something else. These are the severe cases that have not responded to Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT) so those treatments cannot be that effective. Dr.

Speight has seen about seven of these, they are bed-ridden, have very severe unpleasant symptoms, have severe sleep problems and five of them are tube fed because they are too tired to chew and swallow. Dr. Polo mentioned immunoglobulin, he gave this to all the severe cases and they did remarkably well. According to him immunoglobulin as well as Rituximab deserve re-examination for severe cases.

Many paediatricians can see ME and when they see their first case, they panic. Dr. Speight talked about a girl who had been handed to him by the court. The girl had been subjected to three months of vigorous physiotherapy and had severely worsened. The court eventually asked to rehabilitate her before going home. She was lying in a darkened room, catheterised and in severe pain. If any doctors are in charge of a severe case, he advises them not to panic. A doctor always has a

need to treat and investigate and actually trying too hard and over-investigating and treating with things that do not work, is the worst thing you can do for these patients.

Immunoglobulins is one possibility, antibiotic therapy just in case there is an atypical infection such as Lyme disease, otherwise they just deserve tender love and care for their palliative symptoms.

The last case was a German girl, the worst he had ever seen, treated the same way. She was in hospital, having severe pain, was tube fed and the mother was accused of arguing with the doctors about the treatment being provided. The girl was subjected to an activity regime, where she was put in a wheelchair every day. Dragged out of bed, put in the wheelchair - head strapped to the wheelchair because it kept falling. Shoved around the hospital, she was then exposed to a teacher, then exposed to a psychologist, and then exposed to a physiotherapist. She suffered this treatment month after month after month. Dr. Speight asked the doctor in charge: "Have you got her informed consent for this treatment?" and he said no! Dr Speight asked: "Do you have an assessment of her competence to give consent to this treatment?" Again the answer was no! It was not ethical, but they had a court order and the mother had no rights. Luckily, a nice female judge accepted my evidence and reversed the care order and released the girl from the hospital, restored the mother's parental rights and allowed her to take her daughter home. Only two months after that ordeal you can see the girl returning, she is a smiling girl with glistening eyes, nothing like the girl from the hospital. She has been given no magical treatment, just the respect of her autonomy and human right and the company of people who believe in her.



Nancy Van Hoylandt – Quality of life

As an ME patient (and a patient representative) I asked myself what is 'quality of life'? Looking for a definition I found this on the WHO website: "Quality of life is a broad multidimensional concept

that usually includes subjective evaluations of both positive and negative aspects of life".

For me something crucial was missing in this sentence namely that "Quality of life" also depends on the balance between these positive and negative aspects of your life.



Starting from this perspective, I looked at how Myalgic Encephalomyelitis or ME affects my life.

ME, completely changed my life. I went from an active working mother and wife, with two children - six and nine years old at the time- to a debilitated spouse and mum who could barely make it from her bed to the sofa and back. People around me had no idea what was happening to me and reacted with disbelief and ignorance. My employer kept asking me to work from home, up to the point when I literally felt my brain sparking. My brother said: "If you were working for me, you would've been sacked a long time ago." and my mother kept repeating I had to do more, she said I was lazy. I ended up losing all my friends, hardly saw any relatives and spend my days between four walls in the company of my husband and children.

After a few months my GP sent me to a psychiatrist. The seed of depression was planted. The psychiatrist recommended psychotherapy in a day care facility, so I went. This approach did not seem to work and after six months I was told they could not help me, blaming me for the failure of the therapy. By that time I was a complete wreck and needed more therapy to undo the damage from the first round of psychotherapy. My second psychiatrist would eventually apologise for asking too much, too soon, too fast, explaining to me there was more to my condition than meets the eye.

I also followed months of hydrotherapy and

physiotherapy, the result being none other than getting worse. Falling asleep in the car after therapy was no exception; I was exhausted and needed rest. You do not need to worry, I was not the driver!

Once I rode my bike and was not able to lift my legs from the pedals approaching a red light. I had fallen down with the bike before, for the same reason. The light turned green at the last minute. I do not want to know what would have happened otherwise. After the red light incident I stopped riding my bike because it became too dangerous.

After eight years I was diagnosed. Unfortunately, this did not mean getting access to appropriate care, treatment, necessary benefits, etc. The lack of suitable care and available treatment leaves much room for a lot of question rather than answers. And the commonly used name, chronic fatigue syndrome, maintains the enormous burden of stigma attached Myalgic Encephalomyelitis and the psychiatric opinion of it.

Having ME effects every part of my daily life. It starts in the morning when I have to get out of bed, when it feels like I have been run over by a truck, to going to bed when I am not able to fall asleep right away and lie awake for hours.

I feel it when I take a shower and I can hardly lift my arms to wash my hair. Or when I am too tired to stand under the shower and need a small stool to sit on or on days when it is really difficult and I ask one of my daughters to help me. On days when I do not have to leave the house I save energy by just walking around in my pyjama, taking no shower and not combing my hair. However, this is something people do not see when they see me.

While getting dressed I use a chair, always! Because I cannot stand for a long time. When I stand up straight for a long time I get dizzy, nauseous, weak, everything gets black before my eyes and it feels like I am going to faint. This is why I usually sit, hang or do something in between.

During the day the pain varies according to the things I do. When I do too much physical or mental

'work' the pain is worse and I may get a fever. When I go to sleep the following nights, it feels like I have a very severe flu and my whole body aches and shivers. Migraines are my constant companion as a result of stepping over my limits. But that limit can be a scent that is too strong, like my daughter's perfume or a light that is too bright like the sun. I used to be better but after every severe migraine attack I never returned to my old level of functioning.

My digestive problems get worse the more I get tired. The fact that my husband cooks is for two reasons.

I cannot manage three pots and pans anymore, and when I do cook I am too tired to eat afterwards.

The hardest symptom for me to deal with is the cognitive impairment. This makes me feel like I am losing my intellectual abilities. The work I do takes an enormous amount of time, I have trouble concentrating, organising my files, my orientation is all over the place, etc.

Due to my disabilities I am hardly capable of doing housework. The tasks I do take weeks, and some things are just impossible to do. Like I said, my husband usually cooks, does the dishes, the ironing, some of the cleaning and sees to it that I get everywhere I need to be.

But, due to financial difficulties, we are not able to afford the necessary help, such as cooking and cleaning, transportation, care, etc.

Most of the supportive treatments and food supplements prescribed to me are not reimbursed. We are adjusting our home ourselves without reimbursed benefits.

I have been put on retirement due to my illness but I do not have any benefits that come with being retired.

ME also has consequences for my family, my husband and children.

I cannot do the things I would like to do with my children because they are not physically possible. I once got angry with my husband because the bus stopped too far from the parking lot and I could not

walk that far anymore. But that was not his fault. I do not qualify for a disabled parking permit because my physical condition is too good.

And my family cannot do what they want to do because they have to be quiet or need to do something they do not want to.

Intimacy is also a problem in ME. Sometimes I joke about this and say: "I'm getting tired just thinking about it." What people do not know is that there is truth in what I say, which causes marriages to fail and patients to get isolated.

Overall, my ME is an invisible disease, people cannot see I am sick and I am usually not showing it. Even on bad days I keep hearing: "You look fine". As an ME patient I have learned pretty quick to shut up and say I was fine no matter how I felt.

On days when I stay at home, I am completely invisible. Like severe ME patients who are bed-ridden and housebound.

Conclusion

From my story you can gather that there are little positive aspects to having ME. However being a volunteer for the Belgian ME Association and the European ME Alliance has brought meaning to my life. Something that had disappeared since my retirement in 2007.

I have watched my life go by because of ME. Not being able to participate in my own life and if I did/do, I pay the price. So I am here to raise awareness and advocate for a disease called ME that hinders people, who are disabled in various degrees included long-term physical, cognitive or sensory impairments, to participate fully and effectively in society on an equal basis with others.



Dr. Louise Brinth – Challenges and care

Dr. Louise Brinth is a medical doctor and said that medical professionals use diagnosis to sort/classify

patients. We use diagnosis to get a shared reality.

It is a common language between patients, medical professionals and the healthcare system. Patients



with more unexplained symptoms, patients with many symptoms do not always have this luxury of a shared reality and a common language. They may not get a diagnosis, they may get many different diagnoses or they may get misdiagnosed. So patients with many unexplained symptoms, ME patients, they are to some degree very often invisible. They do not pop-up in our studies, when we do witness studies and they do not belong to a dedicated medical specialty. When you get a heart attack you go to a cardiologist, when you have ME or symptoms like ME you do not belong to a medical specialty which is a huge problem.

ME has its own WHO ICD-10 diagnose-code G93.3 which puts it in the group of Neurological Disorders. It is a syndrome diagnosis, which means its diagnosis is built on the presence of symptoms and the typical ME symptoms that ME patients will tell you that they have. The symptoms also included in the different diagnostic criteria are, first and foremost, profound fatigue and fatigability, Post Exertional Malaise (PEM) and Post Exertional worsening of all their symptoms. All their symptoms get worse when they exert themselves too much.

We have many different names for this disorder and it is very difficult and almost impossible to ascertain to what degree these diagnostic entities overlap. The medical aetiology is very unclear. A lot

of very exciting research is going on at the moment and we are gathering a piece of the puzzle but we do not have a coherent medical hypothesis so far and we do not have a clear cut diagnostic biomarker for ME. We have very different diagnostic criteria - she thinks there are more than a hundred all together. So, all in all, you can see that this is quite a diagnostic mess.

She has seen ME patients when she was asked to co-author the paper on quality of life in ME patients and it was first and foremost the work of Michael Hvidberg who should have all the credit for this and who sends his regards. He used a questionnaire, a standardised non-disease specific questionnaire, which is used to describe and value health-related quality of life in patients. It is called the EQ-5D-3L and it has five dimensions. It describes:

- mobility
- self-care
- usual activities
- pain and discomfort
- anxiety/depression

and each of these five dimensions can be valued in three levels of severity:

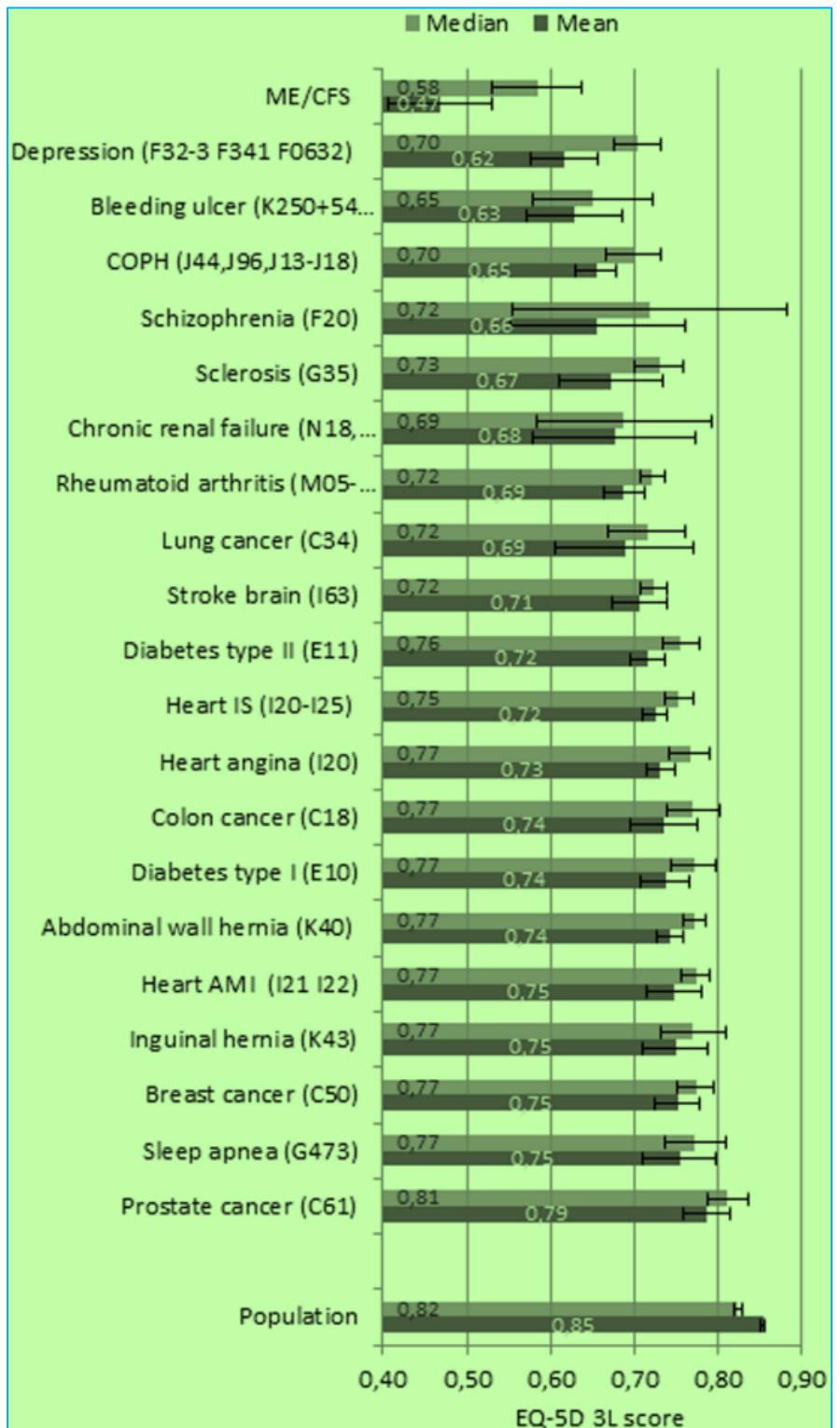
Level 1: indicating no problems whatsoever.

Level 3: signifying severe problems

So, if you have a very good health, no problems, you will score: 1-1-1-1-1

If you are in the worst possible health condition, you will score: 3-3-3-3-3

We got these raw answers from the completed questionnaires, and then based on these each subject is given a single score. One number which is in a linear scale, from - 0.6 to 1- (1 is perfect health and - 0.6 is absolutely terrible health). And this funny scale anchored around zero which equals



death. So if you have a negative value, you have a health state that's conceived worse than death.

So we compare 103 Danish ME patients to the average population and we found in line with the others, that the typical ME patient is a woman, and found that the ME patients were significantly higher educated than the average population but they were not significantly more depressed than the average population. And this is actually a quite

important finding because when you hear about the symptoms of ME patients many will at a first glance think, oh maybe they are just depressed, they are a bit tired, a bit withdrawn from everything but these patients are NOT depressed! This is not depression, this is something completely different and the patients are not more depressed than the average population. We also found that ME patients are more disabled and socially marginalised than the average population, they have fewer relationships than the average population, they have a very high degree of unemployment (only 8% were employed), and more than half were disability pensioners, 12% reported being bedridden, more than half of them were unable to perform usual daily activities, in line with what Nancy told you about her own life, and 28% reported being in extreme pain or extreme discomfort. When you hear about the symptoms of ME, you may think these are common symptoms, trivial symptoms. It is a bit like a hangover. I also have these symptoms but this is not just being fatigued. This is not triviality, this is extremely ill, and seriously disabled people.

Dr. Brinth told us how they transformed the completed questionnaire into one single score per patient and per subject. So they did that for the ME patients and they got this score of 0.47 and the same has been done for other patient groups in Denmark.

From the results one can see that ME is the category of patients with the lowest score. They score lower and report a lower quality of life than any other condition.

They have a lower quality of life than lung cancer patients, patients with stroke, diabetes, breast cancer, lung disease,

What are the consequences?:

Most patients never regain their pre-morbid level of health and functioning so often they learn to live with their symptoms but few of them regain pre-morbid level of functioning.

ME is a massive burden, not only for the patients

but also for the caregivers, and also for all of us for society as such. And it is difficult to ascertain what the burden is for society because they are invisible, undiagnosed, late diagnosed, misdiagnosed. So we cannot count, do the maths or identify how much money this all costs and how much they are suffering. It is a massive problem.

She said that patients often live outside society. In the beginning we may meet them, as medical professionals, as frustrated and angry patients because they are tossed around from specialty to specialty and seen by all sorts of different doctors without given any information or treatment. We find they live outside society because they give up on us, and they are even afraid of medical professionals because they are afraid of what will happen. Patients very often report that they feel they are met with scepticism and even hostility of care providers.

Conclusion

ME is a debilitating and often chronic disease and it is difficult to estimate – affecting maybe 1,000,000 EU citizens. The disease is very poorly understood and, unfortunately, we have several quite contradictory, explanatory models. Some doctors see an ME-like patient and think this is a functional disorder – that is a patient who converses psychological problems into physiological symptoms. Other doctors, other people see these people as patients with physiological severe immunological, mitochondrial, autonomic dysfunction. We do not have any convincing evidence-based treatments so what do we do with the treatment that makes sense in one of these explanatory models? It may seem very harmful for patients from another explanatory model. Graded Exercise Therapy (GET) makes perfectly good sense if you think these patients are young women converting psychological symptoms into physical symptoms, then it is a good thing to push them but if you think they are multi-system ill patients than you will harm them immensely. So it is a matter of should you challenge the patient or should you shield them?

And this problem is causing a serious controversy

among medical professionals, and causing grief to patients and everybody else too which also is reported by Dr. Olli Polo. And it is very difficult to understand what this controversy is all about when you are no part of it. It is very bad!

In 2015 the American Institute of Medicine (IOM) made a report on ME where they concluded many things based on a very thorough investigation - the main conclusion being that ME is a physiological and NOT a psychological disease.

And, they concluded, we should all agree that ME patients need to be recognized, respected and treated.

Unfortunately, many of the patients Dr. Brinth has met have not been recognized, or respected and they are not treated.

So we need help from the politician, not just for money but we all need to work together to put ME on the agenda and we need to change the culture surrounding these disorders because now it is counterproductive. People are afraid of getting into this business, the patients are afraid of the medical professionals so we have a problem and it is a problem that should affect all of us because it affects many patients!

We cannot afford to just let it be!



Dr. László Lovász – Convention on Rights of Persons with Disabilities (CRPD)

Dr. László Lovász started by introducing himself to the audience. He is a lawyer, a doctor, has a PhD and is the first and only Member of the UN in the Committee on Persons with Disabilities and interested in Biomedical and Technological Development in terms of Disability. He was also interested in learning from the



speakers about the disease area and the activities.

He touched upon three areas:

The Convention itself, Cooperation and coordination in relation to the implementation of the convention, Issues of actively planning and implementation of NGOs

The Convention

The Convention is the first human rights treaty in the 21st century and became a very popular convention among the Member States Parties. More than 160 countries have joined the Convention.

It is very important to know that NGOs themselves played a very important and active role when the Convention was adopted and prepared and that they still do when it comes the standards and the obligations of the Convention being met.

In relation to this he highlighted the essential role of the experts when it comes to dialogue and consultations between State Parties and NGOs because the NGOs are the steer provider of very crucial and valuable information for experts and for the cost-active dialogue during the sessions of the Committee.

He mentioned that all experts can be approached by NGOs and that they are open for information from them specifically about a given country's implementations, procedures and feedbacks

He mentioned that the International Disability Alliance is also an important player when meeting the NGOs.

Governments normally have to learn how to implement the obligations of the Convention via mutual progress, mutual learning and mutual understanding. It is very crucial to realise that there is no perfect country because each and every country has difficulties or challenges in terms of

implementing the Convention.

Cooperation and coordination

The definition of disability is an interesting thing From Art.1 – Purpose of CRPD ('Convention of Rights of Persons with Disabilities') include:

“Persons with disabilities include those who have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others.”

“(e) Recognizing that disability is an evolving concept and that disability results from the interaction between persons with impairments and attitudinal and environmental barriers that hinders their full and effective participation in society on an equal basis with others”

h) Recognizing also that discrimination against any person on the basis of disability is a violation of the inherent dignity and worth of the human person,

(i) Recognizing further the diversity of persons with disabilities,

(j) Recognizing the need to promote and protect the human rights of all persons with disabilities, including those who require more intensive support,

Mutual cooperation is important because the Convention strengthens the aspect of international cooperation in Art. 32. The recognition of the importance of independent living and understand reasonable accommodation in an ageing society is not a burden but rather an opportunity. But how because it is a crucial problem we need to fight.

Understanding the spirit of the CRPD in terms of research

(g) To undertake or promote research and development of, and to promote the availability and use of new technologies, including information and communications technologies, mobility aids, devices and assistive technologies, suitable for persons with disabilities, giving priority to

technologies at an affordable cost – Art. 4 – general obligation

Recognition of available good practices and possible overlapping interest

Art. 4 is quite relevant to the recommendation of good practices we all already heard today because when it comes to more efficient lobby work and the current situation of the EU approach towards rare diseases including the existing cooperation among Member States is very important to understand.

Planning and implementation

Identifying trends in technology, societal phenomenon and legislative and non-legislative procedures in the EU Parliament in order to visualise and understand how the international bodies and United Nations operate. In relation to this it is important to present and identify the costs and benefits to society and the communities. It is also worthwhile to explain what happens if more people can contribute to society.

ME STORY

“I have since been sent to another neurologist after my doctor found I was Rhomberg's positive, who made me walk, did a scratch test on my feet, checked the weakness in my legs, and said quite rudely, "you have ME, I am not going to waste time doing tests on you"”

And that was it. I walked away feeling like I had wasted this man's time. I pray one day a cure will come our way.”

- Rowan “Personal Stories of ME Sufferers “

<http://www.investinme.org/mestorygallery1.htm>

The European ME Alliance

The European ME Alliance is a collaboration of ME support charities and organisations in Europe who intend to provide a common view and the scientific facts regarding the neurological illness myalgic encephalomyelitis (ME/CFS).

The alliance has been created with a basic set of principles (see EMEA principles and rules regarding membership).

The members of the European ME Alliance are currently from Iceland, Norway, Sweden, Finland, Denmark, Germany, Holland, Belgium, Switzerland, Italy, Spain, UK and Ireland.

The objectives of the European ME Alliance are to provide a correct and consistent view of myalgic encephalomyelitis (ME/CFS) for healthcare organisations, healthcare professionals, government organisations, the media and patients and the public.

Our web site will consist of accurate descriptions of the illness and details of research which has or is taking place.

The member groups in the alliance will be working together to promote awareness of ME/CFS and will work closely with organisations and researchers who are interested in finding treatments and cures for ME/CFS.

EMEA Principles

The members of the European ME Alliance have agreed the following –

- That members of the European ME Alliance endorse the principles of the 2003 Canadian Consensus Document for Diagnosis and Treatment for ME/CFS.
- That members of the European ME Alliance endorse the principles of the 2006 paediatric definition from Dr www.investinme.org



Leonard Jason et al.

- That members of the European ME Alliance promote the fact that ME (myalgic encephalomyelitis) is a neurological illness in the World Health Organisation's International Classification of Diseases.
- The members of the European ME Alliance understand the necessity to use the composite term ME/CFS at the moment for ease of reference/standardisation.
- The members of the European ME Alliance support biomedical research into establishing sub groups of ME/CFS which will lead to treatments and cures for this illness.
- That the European ME Alliance has, as an objective, the preparation and promotion of a common set of documentation, in all languages, for Alliance use that is supplemented by local information.

<http://www.euro-me.org>



Small Charity BIG Cause

Support ME Awareness
Invest in ME
Research

www.investinme.org



Invest in ME Research (IIMER) was set up with the objectives of making a change in how ME is perceived and treated in the media, by health departments and by healthcare professionals. We aim to do this by finding, funding and facilitating biomedical research, educating healthcare and lobbying for change in policies toward ME.

Invest in ME

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Invest in ME Research

Invest in ME Research

Invest in ME Research

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Invest in ME Research

<https://www.justgiving.com/investinm-e>



#IIMEC12 PRESENTERS



Keynote Speech

Professor Ian Charles

Leader Quadram Institute, Norwich, UK

Professor Ian Charles joined the Institute of Food Research in May 2015 to lead the programme to develop the UK's new Centre for Food & Health – the Quadram Institute - to be based at the Norwich Research Park. He returned to the UK from Australia where he was Director of the itthree institute, University of Technology, Sydney.

Professor Charles has over 30 years' experience in academic and commercial research. His academic career has included being a founding member of The Wolfson Institute for Biomedical Research at University College London, one the UK's first institutes of translational medicine.

He has also worked in the pharmaceutical industry at Glaxo Wellcome, and has been founder and CSO of biotech companies in the area of infectious disease, including Arrow Therapeutics, sold to AstraZeneca, and Auspherix a venture capital backed company founded in 2013.

His current research interests include infectious diseases as well as the microbiome and its impact on health and wellbeing.

The new Centre for Food & Health will provide a step change for food and health research, and the translation of science by industry, to benefit society and the UK economy.

The Centre will be located at the Norwich Research Park, one of Europe's largest single-site concentrations of research in Food, Health and Environmental sciences.

The multidisciplinary Centre aims to bring together the Institute of Food Research and aspects of the University of East Anglia's Faculty of Science and the Norwich Medical School with the regional gastrointestinal endoscopy facility at the Norfolk and Norwich University Hospital. With a unique integration of diet, health, nutrition and medicine under one roof, linking closely to world class plant and crop research at the John Innes Centre and bioinformatics at The Genome Analysis Centre (both also located on the Norwich Research Park), it will have the potential to deliver clinically validated strategies to improve human health and wellbeing.

Abstract:

Not available at time of going to press.

Abstract for IIMEC10 Conference in 2015 -

<http://investinme.org/Documents/Journals/Journal%20of%20IIME%20Vol%209%20Issue%201.pdf>



Keynote Speech

Dr Vicky Whittemore

Program Director in the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in the United States

Dr. Whittemore is a Program Director in the Synapses, Channels and Neural Circuits Cluster. Her interest is in understanding the underlying mechanisms of the epilepsies including the study of genetic and animal models of the epilepsies.

The major goal is to identify effective treatments for the epilepsies and to develop preventions. Dr. Whittemore received a Ph.D. in anatomy from the University of Minnesota, followed by post-doctoral work at the University of California, Irvine, and a Fogarty Fellowship at the Karolinska Institute in Stockholm, Sweden.

She was on the faculty of the University of Miami School of Medicine in The Miami Project to Cure Paralysis prior to working with several non-profit organizations including the Tuberous Sclerosis Alliance, Genetic Alliance, Citizens United for Research in Epilepsy (CURE), and the National Coalition for Health Professional Education in Genetics (NCHPEG). She also just completed a four-year term on the National Advisory Neurological Disorders and Stroke Council.

Abstract:

NIH Research Into ME

Vicky Whittemore, PhD National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA

Significant progress is being made on many research fronts impacting individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

Dr. Whittemore will highlight recent scientific findings from investigators supported by research grant awards from the National Institutes of Health (NIH) and the need for expansion of collaborative research on ME/CFS.

In addition, she will provide an update on NIH research funding plans on ME/CFS, including continued support of investigator-initiated research grants and support for the new ME/CFS Collaborative Research Centers and ME/CFS Data Management Coordinating Center.

She will provide updates on other NIH activities, including the ME/CFS Intramural Research Study, ME/CFS stakeholder conference calls, and activities of the Trans-NIH ME/CFS Working Group and the CFS Advisory Committee (CFSAC).



Professor Sonya Marshall-Gradisnik

The National Centre for Neuroimmunology and Emerging Diseases (NCNED), Griffiths University, Australia

Professor Marshall-Gradisnik is one of Australia's foremost researchers in the area of neuroimmunology and has been instrumental in establishing the Public Health and Neuroimmunology Unit (PHANU) at Bond University.

Much of her work relates specifically to autoimmunity in Chronic Fatigue Syndrome sufferers and she is regularly asked to speak to community groups on behalf of Queensland Health and NSW Health. Her research in the area of exercise immunology has also contributed to the body of knowledge relating to the effect of doping in sport and she serves as Sports Medicine Australia's national spokesperson in this area.

The vital research conducted by Professor Marshall has attracted more than \$1 million in grant funding and she has produced 21 peer-reviewed papers, five book chapters and one provisional patent.

In 2008 Dr Marshall was joint leader of the Bond University team responsible for developing the BioSMART program. The team was awarded a prestigious Australian Teaching and Learning Council Award (formerly known as the Carrick Award) for Outstanding Contribution to Student Learning and for the quality of student learning over a sustained period of time.

Professor Marshall-Gradisnik leads The National Centre for Neuroimmunology and Emerging Diseases (NCNED), a research team situated at Griffith University on the Gold Coast. The team focuses on Myalgic Encephalomyelitis.



Professor Donald Staines

The National Centre for Neuroimmunology and Emerging Diseases (NCNED), Griffiths University, Australia.

Professor Staines has been a public health physician at Gold Coast Population Health Unit. He has worked in health services management and public health practice in Australia and overseas. His interests include collaborative health initiatives with other countries as well as cross-disciplinary initiatives within health. Communicable diseases as well as post infectious fatigue syndromes are his main research interests.

A keen supporter of the Griffith University Medical School, he enjoys teaching and other opportunities to promote awareness of public health in the medical curriculum. He is now Co-Director at The National Centre for Neuroimmunology and Emerging Diseases (NCNED), Griffiths

University in Australia.

Abstract:

Impaired calcium mobilization and dysregulation of transient receptor potential melastatin 3 ion channels in natural killer cells from chronic fatigue syndrome/myalgic encephalomyelitis.

Staines, D.R.^{1,2}, [Nguyen](#), T.,^{1,2}, Johnston, S.^{1,2}, Smith, P.² and Marshall-Gradisnik, S.^{1,2}

1. School of Medical Science, Griffith University, Gold Coast, Australia

2. The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, Australia.

Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (CFS/ME) is disorder with hallmarks of varying changes in immune cells and molecular related mechanisms. Transient receptor potential melastatin subfamily 3 (TRPM3) ion channels play a role in calcium (Ca²⁺) cell signalling. Reduced TRPM3 protein expression has been identified in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) patients. However, the significance of TRPM3 and association with intracellular Ca²⁺ mobilization has yet to be determined. Ca²⁺ flux, TRPM3 and NK cytotoxicity activity was measured under various stimulants, including pregnenolone sulphate (PregS), thapsigargin (TG), 2-aminoethoxydiphenyl borate (2APB) and ionomycin on CD56^{dim}CD16⁺NK cells and CD56^{bright}CD16^{dim/-} isolated NK cells.

Unstimulated CD56^{bright}CD16^{dim/-} NK cells showed significantly reduced TRPM3 receptors in CFS/ME compared with healthy controls (HC). PregS-stimulated CD56^{dim}CD16⁺ NK cells increased TRPM3 expression significantly in CFS/ME, but this was not associated with a significant increase in Ca²⁺flux and NK cell lysis. TG-stimulated CD56^{dim}CD16⁺ NK cells significantly increased NK cell lysis prior to PregS stimulation in CFS/ME patients compared with HC.

Differential expression of TRPM3 and Ca²⁺ flux between NK cell subtypes may provide evidence for their role in the pathomechanism involving NK cell cytotoxicity in CFS/ME.



Professor Nancy Klimas

Director, Institute for Neuro Immune Medicine, Nova Southeastern University

Director, Clinical Immunology Research, Miami VAMC

Professor of Medicine, Department of Clinical Immunology, College of Osteopathic Medicine, Nova Southeastern University

Chair, Department of Clinical Immunology, College of Osteopathic Medicine, Nova Southeastern University

Professor Emerita, University of Miami, School of Medicine

Nancy Klimas, MD, has more than 30 years of professional experience and

has achieved international recognition for her research and clinical efforts in multi-symptom disorders, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), Gulf War Illness (GWI), Fibromyalgia, and other Neuro Immune Disorders. She is immediate past president of the International Association for CFS and ME (IACFS/ME), a professional organization of clinicians and investigators, and is also a member of the VA Research Advisory Committee for GWI, the NIH P2P CFS Committee, and the Institute of Medicine ME/CFS Review Panel. Dr. Klimas has advised three Secretaries of Health and Human Services, including Kathleen Sabelius, during her repeated service on the Health and Human Services CFS Advisory Committee. Professor Klimas has been featured on Good Morning America, in USA Today and the New York Times.

Abstract:

The Gene Study – a Patient Science Partnership Goes Viral

Nancy Klimas, MD 1,2 , Kelly Gaunt Hilton, OMS-III 1 , Kristina Gemayel, OMS-IV1 ,Melanie Perez3 , Rajeev Jaundoo3, Travis Craddock1, Lubov Nathanson PhD1

1Nova Southeastern University College of Osteopathic Medicine, Ft Lauderdale Florida

2 Miami Veterans Medical Center, Miami FL

3 Nova Southeastern University Hamlos College of Natural Sciences and Oceanography

The ME/CFS Gene study is truly unique. Two medical students were challenged to create a study using a social media based platform to ask one of the biggest unanswered questions of our time: what are the genetic underpinnings that put a person at risk for ME/CFS? Why would one person recover from a common infection and the next spin into a chronic disabling illness? Does the genetic signature give us new clues to predict therapies? The challenge was a big one – it takes several thousand volunteers and an expensive genetic assay, then complex analysis to begin to answer questions of genetic risk. The budgets of these studies exceed NIH and foundation caps for funding, and access to that many subjects simply has not happened yet. The study group partnered with advocacy groups across the country and created a novel design: ask patients to donate data not dollars. Use social networking to reach out to the community and ask for access to data from genetic studies that are becoming increasingly common in our society: genomic ancestry platforms.

Millions of people have taken advantage of the ancestry platforms at their own expense to have studies of genetic signatures completed. We are asking ME/CFS patients to donate their data to launch the gene study. Using 23 and Me or Ancestry.com data sets owned by the volunteers, we asked that they log on to our study site, review and sign the informed consent, then take the surveys that ask about their illness, its severity, the way it started etc. At the end they upload the raw data sets from their ancestry studies. More student power is then employed to align the data in spread sheets, then check its quality. Students working with Dr. Lubov Nathanson the gene targets are reviewed for function and likelihood that they would indeed impact important pathways that effect cell function. Then we start with analysis – at this point we have enough data to query specific pathways, asking questions about specific genes, but we do not have enough data to ask the larger questions, find the surprises locked in the gene set that could lead to the “eureka” moments.

We need the effort to go viral to be truly successful, and we need your help. We have 800 volunteers so

far, about half have uploaded the gene data. But we need several thousand to ask the most important questions. So link everyone you know to the website: <http://www.nova.edu/nim/research/mecfs-genes.html> or email: MECFSGenes@nova.edu.

And feel good about this study as it is proof that patient driven, patient sponsored research can lead the way to new treatments. The Blue Ribbon Fellowship, provided by the Blue Ribbon Foundation and the Wisconsin ME/CFS Association, sponsored fellowships for medical students to create the platform and the social media outreach campaign. Patients and advocates helped launch this study and continue to help us promote it. And of course patients and advocates are the participants needed to make this successful. If anyone in the patient community would use their social media skills to get the word out, we could do something truly remarkable: through your efforts partnered with this new generation of physician scientists, answer questions that have been waiting to be answered for far too long.



Dr Jakob Theorell

Jakob Theorell started his medical training at Karolinska Institutet in 2007. He is currently enrolled in the MD-PhD Program at Karolinska Institutet.

He works in the Yen-an Bryceson Group in Karolinska Institutet in Stockholm.

His work focuses on understanding the mechanisms of disease in patients suffering from chronic immunodeficiency syndromes.

The Yen-an Bryceson Group is based at the Center for Infectious Medicine and employs a wide range of techniques including multiparameter flow cytometry, confocal microscopy, live-cell imaging, next-generation sequencing, and biochemical techniques. To gain clinical and scientific insights into human diseases, we collaborate closely with clinicians at Karolinska Institutet, across Scandinavia and the rest of the world.

Abstract:

Myalgic encephalomyelitis or chronic fatigue syndrome (ME/CFS) is a debilitating disorder linked to diverse intracellular infections. Cytotoxic lymphocytes combat intracellular infections. Multiple studies have investigated cytotoxic lymphocyte phenotype and function in ME/CFS, but their specific role in this disorder remains to be established. Prompted by advances in the understanding of defects in lymphocyte cytotoxicity, we aimed to re-assess the role of cytotoxic lymphocytes in ME/CFS, especially for biomarker purposes. To this end, 48 patients fulfilling both Fukuda and Canada criteria for ME/CFS from two independent cohorts were investigated. The phenotype and function of cytotoxic lymphocytes in frozen and thawed PBMC was evaluated by flow cytometry, one cohort at the time. Results were compared to values obtained from simultaneous analysis of cells from age- and sex matched healthy controls. Consistent differences between patients and controls were not found in cytotoxic lymphocyte numbers, cytotoxic granule content, activation status, exocytotic capacity, target cell killing, cytokine production or reprogrammed NK cell expansions. No clear subgroups were identified in unsupervised

dimensionality reduction analyses. One patient showed lower levels of perforin, explained by homozygosity for the PRF1 p.A91V variant, previously associated to haematological malignancies. Among the other patients however, this variant was present in heterozygous state at the expected population frequency, and no additional homozygous carriers were identified. In summary, the results of this study does not support the use of NK cell function as a biomarker for ME/CFS. Furthermore, it does not point to a general role for defects in lymphocyte cytotoxicity in the etiology for ME/CFS.



Professor Geraldine Cambridge

Dr Jo Cambridge is Professorial Research Associate, Div of Medicine Faculty of Medical Sciences, UCL

Her group focuses its interests on B cell depletion (an idea which they introduced (with the Professor Jo Edwards) approximately 10 years ago for the treatment of rheumatoid arthritis), exploring more precisely how the technique works and trying to explain the marked variation in response between different patients



Fane Mensah

Fane Mensah is a research assistant and PhD student studying the immunology of ME in Dr Jo Cambridge's group at UCL.

Fane's main area of study is B-cell research.

Abstract:

Not available at time of going to press.



Professor Simon Carding

Leader, Gut Health and Food Safety Programme Institute of Food Research, Norwich Research Park, UK

Professor Simon Carding Professor of Mucosal Immunology at University of East Anglia and Institute of Food Research. Following his PhD at London he held postdoctoral positions at New York University School of Medicine, New York and at Yale University School of Medicine, New Haven, USA. He then moved to the University of Pennsylvania, Philadelphia, USA as Assistant and later Associate Professor. He joined University of Leeds as Professor of Molecular Immunology in the Institute of Molecular and Cellular Biology in 1999. His scientific interests are in understanding how the immune response in the gut functions and in particular, is able to distinguish between the commensal microbes that reside in the gut and environmental microbes that cause disease, and in the mechanisms by which the body's immune system no longer ignores or tolerates commensal gut bacteria and how this leads to immune system activation and inflammatory bowel disease.

Abstract:

Not present at time of going to press.



Associate Professor Mady Hornig

Associate Professor, Center for Infection and Immunity (CII), Columbia University Mailman School of Public Health New York, USA

Mady Hornig, MA, MD is a physician-scientist in the Center for Infection and Immunity (CII) at the Columbia University Mailman School of Public Health where she serves as Director of Translational Research and is an associate professor of epidemiology.

Her research focuses on the role of microbial, immune, and toxic stimuli in the development of neuropsychiatric conditions, including autism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection), mood disorders and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). She is widely known both for establishing animal models that identify how genes and maturational factors interact with environmental agents to lead to brain disorders and for her work clarifying the role of viruses, intestinal microflora and xenobiotics in autism and other neuropsychiatric illnesses that may be mediated by immune mechanisms.

Under her direction, proteomic analyses of umbilical cord samples are identifying potential birth

biomarkers for autism in a prospective study in Norway, the Autism Birth Cohort (ABC). She established that there was no association between intestinal measles virus transcripts and autism, and, with Brent Williams and W. Ian Lipkin at CII, has found altered expression of genes relating to carbohydrate metabolism and inflammatory pathways and differences in the bacteria harboured in the intestines of children with autism.

She also leads projects examining the influence of immune molecules on brain development and function and their role in the genesis of schizophrenia, major depression, and cardiovascular disease comorbidity in adults, and directs the Chronic Fatigue initiative Pathogen Discovery and Pathogenesis Project at CII. In 2004, Dr. Hornig presented to the Institute of Medicine Immunization Safety Review Committee and testified twice before congressional subcommittees regarding the role of infections and toxins in autism pathogenesis.

Her work in ME/CFS is establishing immune profiles and helping to identify pathogens that may be linked to disease.

Abstract:

Not present at time of going to press.



Professor Olav Mella

Department Director, Oncology, Haukeland University Hospital, University of Bergen, Norway

Professor Mella has performed clinical trials to test the benefit of B-cell depletion therapy using Rituximab in ME/CFS patients. Professor Olav Mella of Haukeland University Hospital in Bergen, Norway began his investigation of Rituximab's effects on CFS after treating several Hodgkin's Lymphoma patients who had long standing cases of CFS prior to developing cancer.

Professor Mella and Dr Fluge have published a paper "Benefit from B-Lymphocyte Depletion Using the Anti-CD20 Antibody Rituximab in Chronic

Fatigue Syndrome. A Double-Blind and Placebo-Controlled Study"

Abstract:

Status of the Norwegian drug intervention studies on ME (RituxME and CycloME)

Olav Mella: for the Norwegian cooperative trial group at Haukeland University Hospital (Bergen), Oslo University Hospital, Telemark Central Hospital – Notodden, St. Olav Hospital (Trondheim) and University Hospital of Northern Norway (Tromsø)

Haukeland University Hospital has previously performed studies indicating that immune manipulation by B-lymphocyte depletion may result in symptom improvement in a subgroup of patients with ME, pointing at defects in immune function to be important factors in the disease mechanisms. Following

previous Phase II studies with the B-cell depleting CD20 monoclonal antibody rituximab, a decision was made to conduct a Norwegian multicenter, Phase III, double blind, placebo controlled intervention study with rituximab, given mainly as outpatient treatment at Day 0 and 14, and at 3, 6, 9 and 12 mths, with follow-up for 24 mths. The number of patients fulfilling Canadian criteria to be recruited at each hospital was predefined, and there was block-randomization to reduce possible practice differences between institutions. The first of the patients started infusion in September 2014, the last patient in September 2015. One primary endpoint is the course in changes of subjectively measured fatigue over 24 mths, with retrospective registration of symptom changes from baseline, every two week periods through follow-up. The other primary endpoint is number of patients achieving clinical response according to predefined criteria. Secondary endpoints are quality of life (SF 36, FSS), changes in physical performance (electronically recorded for 5-7 consecutive days), physical function level at 6, 12, 18 and 24 mths, length of response duration, and patients still in response 24 mths after inclusion. Toxicity is also a secondary endpoint. There is external monitoring of the trial, with full insight into the data.

152 patients were enrolled, but one withdrew before start, leaving 151 evaluable patients. The trial has been performed according to the protocol. There have been hospital admissions, but the safety committee has reported no serious and unexpected toxicity. The randomization and data handling was done through a professional trials company (Viedoc) and the quality of data is judged good by the external monitors.

The final follow-up of the last included patient in the trial will be at the end of September 2017. After that the data quality will be checked and locked, thereafter the trial key unlocked and the study analysed. Publication is expected in 2018.

Based on a small pilot study, the open-label Phase II (CycloME) cyclophosphamide intervention study with 40 patients at two centers was initiated in March 2015. The trial includes patients previously exposed to rituximab, and patients without previous immune manipulation. The patients were given infusions of the cytotoxic agent cyclophosphamide 600-700 mg/m² every 4th week, given 6 times. Endpoints were as in the RituxME study, with follow-up for 18 mths. The last patient will have finished follow-up in July 2017 and the data then analyzed. Compliance has been good, with practically no hematologic toxicity. However, acute nausea and vomiting was experienced to a greater extent than seen in cancer patients at the same drug level, and some patients reported initial and transient worsening of ME-symptoms after infusions. Patients reporting improvement from ME-symptoms generally did so after the final infusion. Although the data has not officially been analyzed, a preliminary observation is that also a more unspecific, immune modulating agent than rituximab can improve the clinical course, in a subgroup of ME patients.

Trial sponsors: Norwegian Research Council, Norwegian Ministry of Health and Care Services, the Regional Health Trusts, MEandYou fundraising, the Norwegian ME Association, private donations, the Kavli Foundation



Dr Øystein Fluge

Chief Physician, Department of Oncology, Haukeland University Hospital, University of Bergen, Norway

Dr Øystein Fluge received medical degree in 1988 at the University of Bergen, and is a specialist in oncology since 2004. He has worked as a Research Fellow with support from the Norwegian Cancer Society and is now chief physician at the Cancer Department, Haukeland University Hospital. Doctoral work emanates from the Surgical Institute and Department of Molecular Biology, University of Bergen.

Abstract:

Metabolic profiling indicates impaired pyruvate dehydrogenase function in ME/CFS patients

Øystein Fluge, Department of Oncology, Haukeland University Hospital, Bergen, Norway.

Metabolic dysfunction has emerged as a plausible contributing factor to ME/CFS. Previous studies have shown reduced levels of selected amino acids in serum or urine from ME/CFS patients. We hypothesized that changes in serum amino acids may disclose specific defects in energy metabolism in ME/CFS.

Analysis in 200 ME/CFS patients and 102 healthy individuals showed a specific reduction of amino acids that fuel oxidative metabolism via the tricarboxylic acid (TCA) cycle. The levels of amino acids that may convert to acetyl-CoA independent of pyruvate dehydrogenase (PDH), and also of anaplerotic amino acids that may replenish TCA cycle intermediates thus increasing the cycle capacity, were particularly reduced mainly in female ME/CFS patients. Amino acids that may convert to pyruvate, and are dependent on PDH for oxidation in the TCA cycle, were not reduced in ME/CFS patients. Serum 3-methylhistidine, a marker of endogenous protein catabolism, was significantly increased in male patients.

The amino acid pattern suggested functional impairment of pyruvate dehydrogenase (PDH), supported by increased mRNA expression of the inhibitory PDH kinases (PDKs) 1, 2 and 4, sirtuin 4, and of peroxisome proliferator-activated receptor δ , in peripheral blood mononuclear cells from both genders.

Myoblasts grown in presence of serum from patients with severe ME/CFS showed metabolic adaptations, including increased mitochondrial respiration and excessive lactate secretion. The pattern of amino acid changes could not be explained by symptom severity, disease duration, age, body mass index, or physical activity level among patients.

These data support a metabolic “obstruction” in the central energy pathway in ME/CFS, a functional impairment possibly at the PDH level with difficulties in metabolizing glucose to energy in the TCA cycle, and with compensatory use of alternative substrates for acetyl-CoA such as ketogenic amino acids and fatty acids. Presently, we are investigating lipid alterations and B-vitamins in the same serum samples. We hypothesize that the inhibition of energy metabolism is caused by an aberrant immune response, in a subgroup of ME/CFS patients with a central role for B-cells and possibly antibodies.

These findings are in agreement with the clinical disease presentation of ME/CFS, with inadequate ATP

generation by oxidative phosphorylation and excessive lactate generation upon exertion.



Professor Warren Tate

Group Leader, Biochemistry Department, School of Biomedical Sciences, University of Otago, New Zealand

Professor Warren Tate from University of Otago in New Zealand - is an internationally respected biochemist, winner of the Royal Society of New Zealand's top science honour - the 2010 Rutherford Medal, and was also named a Companion of the New Zealand Order of Merit. His honour citation noted that Professor Tate was a molecular biologist, whose research had "revolutionised understanding" of how proteins were synthesised in living cells. His research had shown how proteins contributed to memory formation and neurological disease, and had important implications for HIV, Alzheimer's and chronic fatigue syndrome. Professor Tate is a Fellow of the Royal Society of New Zealand and of the New Zealand Institute of Chemistry. He has been a Fellow of the Alexander von Humboldt Foundation of Germany, and an International Research Scholar of the Howard Hughes Medical Institute of the United States.

Abstract:

Intense molecular study of well characterised patients to understand the acute phase, perpetuation, and relapse/recovery cycles in ME/CFS

Warren P. Tate, Department of Biochemistry, School of Biomedical Sciences, Division of Health Sciences, University of Otago, PO Box 56 Dunedin, New Zealand

From the moment of my first exposure over 20 years ago to ME/CFS as the illness afflicting a vibrant young teenage daughter, I have puzzled over what physiological 'control centre' could mediate such a range of dramatic body-wide responses. As my daughter's illness progressed into a long-term condition this question evolved into what is preventing recovery and not allowing perpetuation of ME/CFS, and then what physiological changes are occurring during the frequent relapses experienced throughout the chronic phase of the disease. On a brighter note a significant improvement occurred during a pregnancy –why did that happen? Resolution of these unresolved yet important questions would give significant benefit to patients, as well as being of marked scientific interest.

As research into ME/CFS has progressed in recent decades there has been a pressing need to collect comprehensive molecular data on well-characterised patients so a framework can be created for evidence-based approaches to the disease. This would have relevance for developing a diagnostic test, and to set directions towards better patient management and therapies. We have studied purified

blood fractions from two small patient cohorts, each of 10 patients with age and gender matched controls, one of which was focussed on exercise intolerance and 'post exertion malaise'. Initially we collected data on the immune cell expressed genes (transcriptome) and proteins (proteome) as well as plasma microRNAs and cytokines with an aim of integrating the data to elucidate linkages between different classes of molecules and give insight into physiological changes. We are currently extending these studies to mitochondrial function and epigenetic changes in the DNA following the recently published research suggesting energy delivery and modulation of expression of specific genes might be significant factors in changes in physiology for perpetuation of the disease.

Can a model be developed that might explain most of the diverse symptoms? Evidence of chronic inflammation in the limbic system of the brain and glial cell activation has been shown in neuroimaging studies of Japanese ME/CFS patients, with a degree of inflammation that correlated with severity of disease symptoms. These observations, coupled with the known disturbance of the hypothalamus/pituitary/adrenal axis in ME/CFS, and the hypersensitivity of ME/CFS patients to stress of any kind, has lead us to develop a model whereby the paraventricular nucleus (PVN), the 'stress centre' of the hypothalamus, might be a possible ME/CFS perpetuating centre. The PVN is responsible for absorbing and processing incoming stress signals and chronic fluctuating auto-inflammation in the brain affecting the threshold for managing stress could explain perpetuation of the disease and relapses in the chronic phase of ME/CFS.

Detailed molecular and neuroimaging data from patients using cutting edge technologies will allow new models to explain ME/CFS and should provide meaningful benefits for patients for managing and living with their disease.



Professor Ron Davis

Professor of Biochemistry and Genetics at the Stanford School of Medicine in Stanford, California, USA

Ronald W. Davis, Ph.D., is a Professor of Biochemistry and Genetics at the Stanford School of Medicine in Stanford, California.

He is a world leader in the development of biotechnology, especially the development of recombinant DNA and genomic methodologies and their application to biological systems.

At Stanford University, where he is Director of the Stanford Genome Technology Center, Dr. Davis focuses on the interface of nano-fabricated solid state devices and biological systems.

He and his research team also develop novel technologies for the genetic, genomic, and molecular analysis of a wide range of model organisms as well as humans.

The team's focus on practical application of these technologies is setting the standard for clinical

genomics.

Abstract:

Establishing new mechanistic and diagnostic paradigms for ME/CFS

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is the last major disease we know almost nothing about. To date, very little is understood about the cause of ME/CFS: years of searching for a common triggering pathogen have been fruitless, and no biological assays exist to facilitate diagnosis. Recent evidence strongly supports ME/CFS as a molecular disease, even if many of the symptoms are cognitive and muscular, which indicates that molecular studies will help to understand and diagnose this disease, and that molecular therapies have the potential to treat it. The time is ripe for this change in perspective, because researchers now have highly advanced, sensitive, and comprehensive molecular technologies at their disposal, and the beginnings of a molecular understanding with which to unravel this disease. We are working to unravel the molecular path from health to ME/CFS, and develop cost-effective technology for diagnosis and drug discovery – offering a new level of precision for researchers and physicians to tackle this complex illness. All of this research is being carried out in close collaboration with physician, patient, and advocate communities, including direct involvement of patient partners and dedicated outreach efforts to broaden awareness of the disease.

We aim to implement an interdisciplinary, integrative, inclusive precision approach to ME/CFS to fundamentally change how this disease is understood and managed, and most importantly, to give new hope to patients.

Invest in ME Research

International ME Colloquium / Conference London 2017



The 12th IIMER International ME Conference 2017

#IIMEC12 CONFERENCE PROGRAMME

Start	Presenter	Presentation
07.45	<i>Registration</i>	
08.55	Invest in ME Research	Opening
09:00	Dr Ian Gibson	Welcome to IIMEC12
09:05	Professor Ian Charles	A UK Centre of Excellence for ME
09:25	Dr Vicky Whittemore	Keynote Speech: NIH Research into ME
09:45	Professor Don Staines	Dysregulation of Transient Receptor Potential (TRP) ion channels and calcium in natural killer cells in CFS/ME patients
10:15	Professor Nancy Klimas	Genetic Signature Study
10.45	<i>Break</i>	
11.15	Dr Jakob Theorell	Studies of NK cells and cytotoxic T-cells in ME-patients from one Swedish and one Norwegian cohort
11:40	Dr Jo Cambridge / Fane Mensah	Update on Immunoregulation in patients with ME – new paper immunological review
12.05	Professor Simon Carding	UEA/Quadram Inst. Gut Virome in ME - Students
12.30	<i>Lunch</i>	
13.30	Professor Mady Hornig	Gut-metabolome-immune disturbances in ME/CFS subsets
14:00	Professor Olav Mella	Status of the Norwegian drug intervention studies on ME (RituxME and CycloME)
14:30	Dr Øystein Fluge	Metabolic profiling in ME/CFS
15.10	<i>Break</i>	
15:40	Professor Warren Tate	Intense molecular study of well characterised patients to understand the acute phase, perpetuation, and relapse/recovery cycles in ME/CFS
16.10	Professor Ron Davis	Big Data Approach: Severely ill ME Patient Cohort
17.00	Dr Ian Gibson	Plenary Session
17.30	<i>Adjourn</i>	

Raising Awareness of Myalgic Encephalomyelitis - The European Way

Mike Harley is running **28 European marathons** – raising funds for Invest in ME Research's Centre of Excellence for ME research and raising awareness of this disease. Please help us in supporting Mike

<http://www.investinme.org/ce-IIME-Newslet-1504-02.shtml>



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Let's  research!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. UK Charity Invest in ME - Research (IMER) are establishing a Centre of Excellence for ME - a hub for research activity in Europe - enabling a strategy of high-quality biomedical research projects to follow, coordinated and collaborating with other institutes. Please support our C of E for ME. Let's Do It for ME. Let's C research into ME. See <http://www.investinme.org/research#CofEforME> #LetsCresearch @LetsDolt4ME

Invest in ME - Research (UK charity nr. 1153730)

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